Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

German Edition: DOI:

Tandem *Z*-Selective Cross-Metathesis/Dihydroxylation: Synthesis of *anti*-1,2-Diols**

*Peter K. Dornan, Zachary K. Wickens, and Robert H. Grubbs**

anie_201501505_sm_miscellaneous_information.pdf

Table of Contents

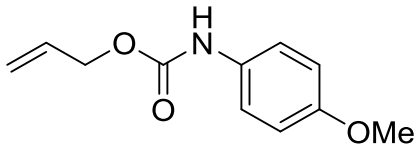
General Information

All metathesis reactions were setup in a Vacuum Atmospheres glovebox under a nitrogen atmosphere. Solvents were purified by passage through solvent purification columns and further degassed with Argon.[1] Commercially available liquid reagents were degassed by three freeze pump thaw cycles (for volatile substrates) or under vacuum (for nonvolatile substrates) prior to entering the glove box. Stock solutions of the cyclometalated ruthenium catalysts were prepared in the glovebox, stored at -35 °C in the glovebox freezer, and used within four weeks. Sodium periodate and $CeCl_3$ heptahydrate were purchased from Aldrich and used as is.

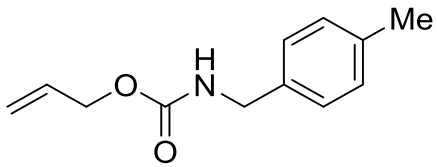
Standard NMR spectroscopy experiments were conducted on a Varian INOVA 500 (^{1}H: 500 MHz, ^{13}C: 126 MHz) or a Bruker Avance HD 400 (^{1}H: 400 MHz, ^{13}C: 101 MHz, equipped with a cryoprobe) spectrometer. Chemical shifts are referenced to the residual solvent peak ($CDCl_3$, C_6D_6 or DMSO-d_6). Multiplicity is reported as follows: (s: singlet, d: doublet, t: triplet: q: quartet, br: broad, m: multiplet). Spectra were analyzed and processed using MestReNova. High-resolution mass spectra were provided by the California Institute of Technology Mass Spectrometry Facility using JEOL JMS-600H High Resolution Mass Spectrometer.

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J., *Organometallics* **1996,** *15,* 1518-1520.

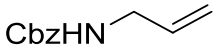
Synthesis of substrates



Allyl (4-methoxyphenyl)carbamate (5e): To a flame dried round bottom flask under argon was added *p*-anisidine (1.85 g, 15 mmol, 1 equiv), CH_2Cl_2 (45 mL) and diisopropylethylamine (2.79 mL, 16 mmol, 1.07 equiv), and the flask was cooled to 0 °C and stirred. Allyl chloroformate (1.70 mL, 16 mmol, 1.07 equiv) was then added dropwise. After 30 min, the flask was allowed to warm to ambient temperature and stirred for an additional 30 min. The reaction mixture was quenched with 20 mL HCl (1M) and extracted with 150 mL EtOAc. The organic extract was then washed with saturated $NaHCO_3$ (20 mL), brine (20 mL), and then dried with Na_2SO_4 and concentrated *in vacuo*. The title compound was isolated by column chromatography (15 – 30% EtOAc in Hexanes) to give a white solid (2.853 g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 9.1 Hz, 2H), 6.52 (br s, 1H), 5.97 (ddt, *J* = 16.9, 10.4, 5.7 Hz, 2H), 5.35 (dd, *J* = 17.2, 1.6 Hz, 2H), 5.25 (dd, *J* = 10.5, 1.3 Hz, 1H), 4.66 (dt, *J* = 5.7, 1.4 Hz, 4H), 3.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 153.7, 132.7, 131.0, 120.8, 118.3, 114.4, 65.9, 55.7. HRMS (FAB+): *m/z* calculated for $[C_{11}H_{13}O_3N]^+$: 207.0895; found: 207.0895.



Allyl (4-methylbenzyl)carbamate (5f): To a flame dried round bottom flask under argon was added 4-methylbenzylamine (1.91 mL, 15 mmol, 1 equiv), CH_2Cl_2 (45 mL) and diisopropylethylamine (2.79 mL, 16 mmol, 1.07 equiv), and the flask was cooled to 0 °C and stirred. Allyl chloroformate (1.70 mL, 16 mmol, 1.07 equiv) was then added dropwise. After 30 min, the flask was allowed to warm to ambient temperature and stirred for an additional 30 min. The reaction mixture was quenched with 20 mL HCl (1M) and extracted with 150 mL EtOAc. The organic extract was then washed with saturated $NaHCO_3$ (20 mL), brine (20 mL), and then dried with Na_2SO_4 and concentrated *in vacuo*. The title compound was isolated by column chromatography (15 – 30% EtOAc in Hexanes) to give a white solid (2.655 g, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 5.93 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.31 (dd, *J* = 17.1, 1.6 Hz, 1H), 5.21 (dq, *J* = 10.5, 1.4 Hz, 1H), 4.99 (br s, 1H), 4.60 (d, *J* = 6.0 Hz, 2H), 4.34 (d, *J* = 5.9 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 137.3, 135.5, 133.0, 129.5, 127.7, 117.8, 65.8, 45.0, 21.2. HRMS (FAB+): *m/z* calculated for $[C_{12}H_{15}O_2N+H]^+$: 206.1181; found: 206.1183.



Benzyl allylcarbamate (5h): Prepared according to a literature procedure, and the spectroscopic data matched the literature data.[2]

[2] H. Teller, M. Corbet, L. Mantilli, G. Gopakumar, R. Goddard, W. Thiel, A. Fürstner, *J. Am. Chem. Soc.* **2012**, *134*, 15331–15342.

General procedures and product characterization

General procedure A: Optimization for tandem Z-selective homodimerization – dihydroxylation: In a nitrogen filled glove box, allyl butyrate (25.6 mg, 0.2 mmol, 1 eq) was transferred to a 25 mL Schlenk tube using three 50 µL portions of a solution of the appropriate metathesis catalyst (0.003 mmol, 1.5 mol%, 150 µL, 0.02M in THF) to ensure quantitative transfer. The tube was capped, and then brought to a Schlenk line where it was evacuated using one freeze-pump-thaw cycle, capping the flask under static vacuum. The solution was then heated in an oil bath with stirring at 40 °C for 4 hr. A solution of the appropriate Lewis acid (10 mol %) in distilled H_2O (170 µL) was added to $NaIO_4$ (42.8 mg, 0.2 mmol, 2 eq relative to the homodimerization metathesis product at full conversion). MeCN (500 µL) was then added, and the mixture was cooled to 0 °C in an ice bath. The crude metathesis mixture was then added, using ethyl acetate (3 x 167 µL) to rinse the flask and ensure complete transfer. The mixture was vigorously stirred at 0 °C for 20 min and then quenched with 2 mL of a saturated $Na_2S_2O_3$ aqueous solution. The mixture was extracted with ethyl acetate (4 x 2.5 mL), and then concentrated under reduced pressure. Mesitylene (27.8 µL, 0.2 mmol) was added as an internal standard, and the mixture was dissolved in $CDCl_3$ for NMR studies (^{1}H NMR, 8 scans, 25 s relaxation delay).

Note: For Table 1, entry 6, ethyl vinyl ether (0.2 mmol, 18.6 µL) was added after the metathesis step, and the mixture was stirred for 20 minutes at ambient

temperature. Subsequently, the volatiles were removed and the mixture was dissolved in ethyl acetate to add to the oxidation mixture.

General procedure B: Z-selective homodimerization under static vacuum. In a nitrogen filled glove box, the terminal olefin was transferred to a 25 mL Schlenk tube using three 50 µL portions of a solution of Ad-DIPP-NO_3 **4** (0.003 mmol, 1.5 mol%, 150 µL, 0.02M in THF) to ensure quantitative transfer. The tube was capped, and then brought to a Schlenk line where it was evacuated using one freeze-pump-thaw cycle, capping the flask under static vacuum. The solution was then heated in an oil bath with stirring at 40 °C for 4 hr.

General procedure C: Z-selective homodimerization in an open vial. In a nitrogen filled glove box, a solution of Ad-DIPP-NO_3 **4** (0.001 mmol, 0.5 mol%, 200 µL, 0.005M in THF) was added to the terminal olefin (0.2 mmol, 1 eq) in a 2 dram vial. The mixture was stirred in an open vial in the glove box at 40 °C for 3 hr.

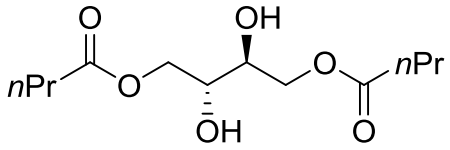
General procedure D: Dihydroxylation for 0.2 mmol scale homodimerizations. A solution of $CeCl_3$ heptahydrate (3.7 mg, 0.01 mmol, 10 mol%) in distilled H_2O (170 µL) was added to $NaIO_4$ (42.8 mg, 0.2 mmol, 2 eq relative to the homodimerization metathesis product at full conversion). MeCN (500 µL) was then added, and the mixture was cooled to 0 °C in an ice bath. The crude metathesis mixture was then added, using ethyl acetate (3 x 167 µL) to

rinse the flask and ensure complete transfer. The mixture was vigorously stirred at 0 °C for 20 min and then quenched with 2 mL of a saturated $Na_2S_2O_3$ aqueous solution. The mixture was extracted with ethyl acetate (4 x 2.5 mL), and then concentrated under reduced pressure. The anti-diol product was purified by column chromatography.

General procedure E: Z-selective cross metathesis in an open vial followed by dihydroxylation. In a nitrogen filled glove box, a solution the excess olefin reagent (0.5 mmol, 5 eq) in THF (150 µL) was added to the limiting olefin reagent (0.1 mmol, 1 eq) in a 2 dram vial. A solution of Ad-DIPP-NO_3 **4** (0.003 mmol, 3 mol%, 150 µL, 0.02 M in THF) was added. The mixture was stirred in the open vial in the glove box at 40 °C for 4 hr. A solution of $CeCl_3$ heptahydrate (11.2 mg, 0.03 mmol) in distilled H_2O (0.5 mL) was added to $NaIO_4$ (128.3 mg, 0.6 mmol). MeCN (1.5 mL) was then added, and the mixture was cooled to 0 °C in an ice bath. The crude metathesis mixture was then added, using ethyl acetate (3 x 0.5 mL) to rinse the flask and ensure complete transfer. The mixture was vigorously stirred at 0 °C for 20 min and then quenched with 6 mL of a saturated $Na_2S_2O_3$ aqueous solution. The mixture was extracted with ethyl acetate (4 x 4 mL), and then concentrated under reduced pressure. The anti-diol product was purified by column chromatography.

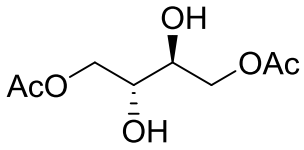
Note: For all substrates, an independent metathesis reaction under identical conditions as the tandem process was performed and the Z-selectivity assessed

by ^{1}H NMR, to ensure that isomerization did not occur in the time scale of the metathesis. Z-selectivity was >90% in all cases. The ^{1}H NMR signals were compared to those observed in an early conversion (30 minute) metathesis reaction, (1 mol% **4**, reaction in an open vial), to aid in peak assignment. In general, static vacuum conditions for the metathesis step were successful in minimizing Z to E isomerization (due to removal of ethylene from solution). An alternative strategy to remove ethylene from the reaction is to perform the metathesis step in an open vial inside an inert atmosphere glove box. This was an effective strategy for substrates which are not volatile and do not become highly viscous or solid upon loss of solvent during cross metathesis. This open vial procedure was used for allyl phenyl carbonate and the hetero cross metathesis / dihydroxylation reactions.

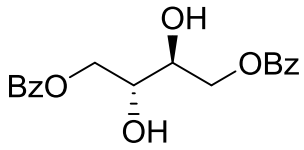


Anti-2,3-dihydroxybutane-1,4-diyl dibutyrate (6a): Synthesized according to the general procedure B for homodimerization under static vacuum followed by the general procedure D for dihydroxylation. The title compound was purified by column chromatography (50-75% ethyl acetate in hexanes). This material was then triturated with ether to afford a white solid (18.8 mg, 72%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.34-4.31 (m, 4H), 3.80-3.75 (m, 2H), 2.90-2.70 (br s, 2H), 2.35 (t, J = 7.4 Hz, 4H), 1.67 (hex, J = 7.4 Hz, 4H), 0.95 (t, J = 7.4 Hz, 6H); ^{13}C

NMR (126 MHz, $CDCl_3$) δ 174.7, 70.6, 65.6, 36.1, 18.5, 13.8. HRMS (FAB+): *m/z* calculated for $[C_{12}H_{22}O_6+H]^+$: 263.1495; found: 263.1490.



Anti-2,3-dihydroxybutane-1,4-diyl diacetate (6b): Synthesized according to the general procedure B for homodimerization under static vacuum followed by the general procedure D for dihydroxylation. The title compound was isolated by column chromatography (60-80% ethyl acetate in hexanes) to give a clear oil (12.2 mg, 59%). Spectroscopic data matched literature data.[3] ^{1}H NMR (400 MHz, DMSO-d6) δ 4.36-4.26 (m, 4H), 3.79 (s, 2H), 2.80 (br s), 2.12 (s, 6H); ^{13}C NMR (101 MHz, CDCl3) δ 172.0, 70.5, 65.8, 21.0; HRMS (FAB+): *m/z* calculated for $[C_8H_{14}O_6+H]^+$: 207.0869; found: 207.0861.

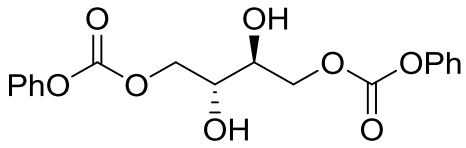


Anti-2,3-dihydroxybutane-1,4-diyl dibenzoate (6c): Synthesized according to the general procedure B for homodimerization under static vacuum followed by the general procedure D for dihydroxylation. The title compound was purified by column chromatography (60-80% ethyl acetate in hexanes). This material was then triturated with ether to afford a white solid (23.4 mg, 71%) which was sparingly soluble in $CDCl_3$ but soluble in DMSO. ^{1}H NMR (500 MHz, DMSO-d_6) δ

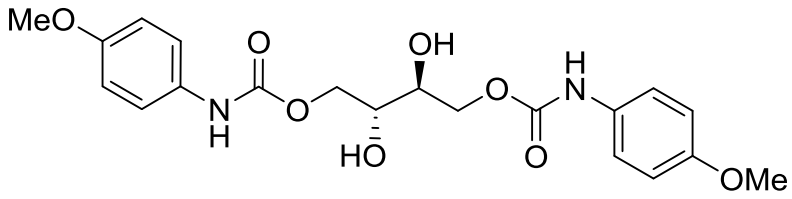
[3] T. K. M. Shing, E. K. W. Tam, V. W.-F. Tai, I. H. F. Chung, Q. Jiang, *Chem. – Eur. J.* **1996**, *2*, 50–57.

8.03 (dd, *J* = 8.4, 1.3 Hz, 4H), 7.66 (tt, *J* = 7.5, 1.5 Hz, 2H), 7.53 (t, *J* = 7.5 Hz, 4H), 5.36 (d, *J* = 5.9 Hz, 2H), 4.50 (dd, *J* = 11.3, 2.1 Hz, 2H), 4.31 (dd, *J* = 11.2, 5.7 Hz, 2H), 3.87-3.83 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.9, 133.3, 130.0, 129.3, 128.7, 69.2, 66.7. HRMS (FAB+): *m/z* calculated for $[C_{18}H_{18}O_6+H]^+$: 331.1182; found: 331.1182.

Procedure for large scale synthesis: In a nitrogen filled glove box, a solution of Ad-DIPP-NO_3 **4** (20.8 mg, 0.0309 mmol, 0.5 mol%) in THF (2.17 mL) was added to allyl benzoate (1.0 g, 6.17 mmol) in a 10 dram vial. The mixture was stirred in an open vial in the glove box at 40 °C for 7.5 hr. A solution of $CeCl_3$ heptahydrate (115 mg, 0.309 mmol) in distilled H_2O (5.1 mL) was added to $NaIO_4$ (1.32 g, 6.17 mmol, 2 eq relative to the homodimerization metathesis product at full conversion) in a round bottom flask. MeCN (15.4 mL) was then added, and the mixture was cooled to 0 °C in an ice bath. The crude metathesis mixture was then added, using ethyl acetate (3 x 5.1 mL) to rinse the flask and ensure complete transfer. The mixture was vigorously stirred at 0 °C for 20 min and then quenched with 25 mL of a saturated $Na_2S_2O_3$ aqueous solution. The mixture was extracted with ethyl acetate (3 x 60 mL), dried with Na_2SO_4 and then concentrated under reduced pressure. The resulting solid was then triterated with diethyl ether (5 x 5 mL) to give the title compound as a white solid (669 mg, 66%).

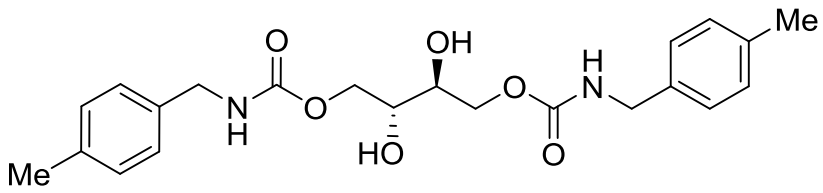


Anti-2,3-dihydroxybutane-1,4-diyl diphenyl bis(carbonate) (6d): Synthesized according to the general procedure C for homodimerization in an open vial followed by the general procedure D for dihydroxylation. The title compound was purified by column chromatography (60–75% ether in pentane) to give a white solid (22.1 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 8.6, 7.3 Hz, 4H), 7.35 – 7.24 (m, 2H), 7.24 – 7.14 (m, 4H), 4.64 – 4.54 (m, 2H), 4.54 – 4.45 (m, 2H), 4.08 – 3.97 (m, 2H), 2.67 (br s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 151.0, 129.6, 126.3, 120.9, 70.0, 69.5. HRMS (FAB+): *m/z* calculated for $[C_{18}H_{18}O_8+H]^+$: 363.1080; found: 363.1081.

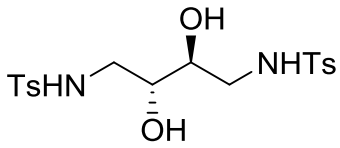


Anti-2,3-dihydroxybutane-1,4-diyl bis((4-methoxyphenyl)carbamate) (6e): Synthesized according to the general procedure B for homodimerization under static vacuum followed by the general procedure D for dihydroxylation. The title compound was purified by column chromatography (80-100% ethyl acetate in hexanes) followed by trituration of the impure fractions with diethyl ether to afford a white solid (26.6 mg, 63%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.45 (br s, 2H), 7.37 (d, *J* = 8.6 Hz, 4H), 6.85 (d, *J* = 8.9 Hz, 4H), 5.07 (d, *J* = 4.8 Hz, 2H), 4.29 (dd, *J* = 11.4, 2.3 Hz, 2H), 4.04 (dd, *J* = 11.1, 5.5 Hz, 2H), 3.70 (s, 6H), 3.7-3.65

(m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 153.9, 132.3, 119.7, 113.9, 69.7, 66.1, 55.1; HRMS (FAB+): *m/z* calculated for $[C_{20}H_{24}O_8N_2+H]^+$: 421.1611; found: 421.1606.

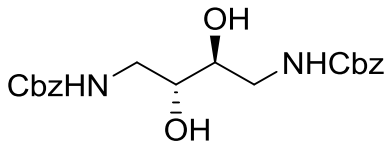


Anti-2,3-dihydroxybutane-1,4-diyl bis((4-methylbenzyl)carbamate) (6f): Synthesized according to the general procedure B for homodimerization under static vacuum followed by the general procedure D for dihydroxylation. The title compound was purified by column chromatography (80% ethyl acetate in hexanes to 10% MeOH in ethyl acetate) followed by trituration with diethyl ether to afford a pale yellow solid (16.4 mg, 39%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (t, *J* = 6.2 Hz, 1H), 7.16-7.08 (m, 8H), 4.93 (d, *J* = 4.9 Hz, 2H), 4.20-4.10 (m, 8H), 3.91 (dd, *J* = 11.4, 5.7 Hz, 2H), 3.57 – 3.51 (m, 2H), 2.27 (s, 6H); ^{13}C NMR (101 MHz, DMSO) δ 156.7, 136.9, 135.7, 128.8, 127.0, 69.9, 66.0, 43.5, 20.7; HRMS (FAB+): *m/z* calculated for $[C_{22}H_{28}O_6N_2+H]^+$: 417.2026; found: 417.2036.

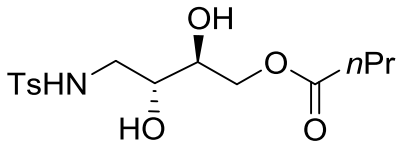


N,N'-((Anti)-2,3-dihydroxybutane-1,4-diyl)bis(4-methylbenzenesulfonamide) (6g): Synthesized according to the general procedure B for homodimerization under static vacuum followed by the general procedure D for dihydroxylation. The title compound was purified by column chromatography (80% ethyl acetate in

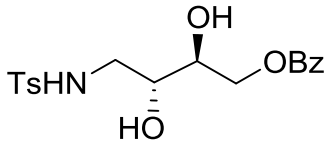
hexanes) to give a white solid (30.1 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, J = 8.2 Hz, 4H), 7.38 (d, J = 8.1 Hz, 4H), 7.28 (dd, J = 6.8, 5.4 Hz, 2H), 4.88 (br s, 2H), 3.23 (d, J = 7.0 Hz, 2H), 2.98 (ddd, J = 12.7, 6.9, 2.2 Hz, 2H), 2.56-2.50 (m, 2H), 2.37 (s, 6H); ^{13}C NMR (126 MHz, DMSO) δ 142.55, 137.52, 129.60, 126.65, 71.26, 46.22, 21.01. HRMS (FAB+) m/z calculated for $[C_{18}H_{24}O_6S_2N_2+H]^+$: 429.1154; found: 429.1175.



Dibenzyl ((Anti)-2,3-dihydroxybutane-1,4-diyl)dicarbamate (6h): Synthesized according to the general procedure B for homodimerization under static vacuum followed by the general procedure D for dihydroxylation. The title compound was purified by column chromatography (60–85% ethyl acetate in hexanes) to give a white solid (20.7 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.34 (m, 10H), 5.25 (br s, 2H), 5.12 (s, 4H), 3.91 (br s, 2H), 3.66 (dd, *J* = 15.0, 7.8 Hz, 2H), 3.46 (s, 2H), 3.30 (d, *J* = 14.8 Hz, 2H). ^{13}C NMR (101 MHz, DMSO) δ 156.8, 137.7, 128.8, 128.2, 128.2, 71.9, 65.7, 44.5. HRMS (FAB+) m/z calculated for $[C_{20}H_{24}O_6N_2+H]^+$: 389.1713; found: 389.1721.

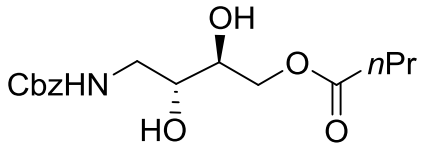


(Anti)-2,3-dihydroxy-4-((4-methylphenyl)sulfonamido)butyl butyrate (6i): Synthesized according to general procedure E for cross metathesis – dihydroxylation using allyl butyrate as the olefin in excess. The metathesis was performed at 35 °C using 1.5 mol% Ru (0.0015 mmol). The title compound was purified by column chromatography (50-70% ethyl acetate in hexanes) to give a white solid (21.8 mg, 63%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 5.51 (t, J = 6.5 Hz, 1H), 4.33-4.22 (m, 2H), 3.82 (br s, 1H), 3.62 (br s, 1H), 3.48 (d, J = 5.5 Hz, 1H), 3.22 – 3.07 (m, 3H), 2.42 (s, 3H), 2.32 (t, J = 7.5 Hz, 2H), 1.63 (hex, J = 7.4 Hz, 2H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 143.9, 136.5, 130.0, 127.2, 71.1, 70.3, 65.6, 45.3, 36.1, 21.7, 18.5, 13.8. HRMS (FAB+) m/z calculated for $[C_{15}H_{23}O_6SN+H]^+$: 346.1324; found: 346.1315.



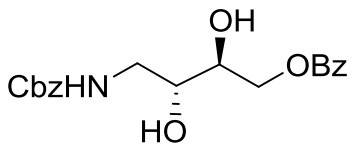
Anti-2,3-dihydroxy-4-((4-methylphenyl)sulfonamido)butyl benzoate (6j): Synthesized according to general procedure E for cross metathesis – dihydroxylation using allyl benzoate as the olefin in excess. The title compound was purified by column chromatography (50-60% ethyl acetate in hexanes) followed by preparatory thin layer chromatography (60% ethyl acetate in

hexanes) to give a white solid (14.6 mg, 39%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.99 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.66 (tt, *J* = 7.6, 1.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.42-7.36 (m, 1H), 7.38 (d, *J* = 7.7 Hz, 2H), 5.16 (d, *J* = 5.7 Hz, 1H), 5.06 (d, *J* = 5.7 Hz, 1H), 4.37 (dd, *J* = 11.3, 2.8 Hz, 1H), 4.18 (dd, *J* = 11.3, 5.8 Hz, 1H), 3.63 – 3.47 (m, 2H), 3.11 (ddd, *J* = 12.7, 6.8, 3.1 Hz, 1H), 2.67 (ddd, *J* = 12.8, 7.7, 5.4 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.8, 142.5, 137.6, 133.2, 129.9, 129.5, 129.3, 128.6, 126.6, 70.3, 70.1, 66.5, 46.4, 21.0. HRMS (FAB+): *m/z* calculated for $[C_{18}H_{21}O_6SN+H]^+$: 380.1168; found: 380.1152.



Anti-4-(((benzyloxy)carbonyl)amino)-2,3-dihydroxybutyl butyrate (6k): Synthesized according to general procedure E for cross metathesis – dihydroxylation using allyl butyrate as the olefin in excess. The title compound was purified by column chromatography (50-70% ethyl acetate in hexanes) followed by preparatory thin layer chromatography (60% ethyl acetate in hexanes) to give a white solid (15.4 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$-d_6) δ 7.39-7.29 (m, 5H), 5.37 (t, *J* = 7.2 Hz, 1H), 5.11 (s, 2H), 4.40 (dd, *J* = 12.0, 4.5 Hz, 1H), 4.34-4.23 (m, 1H), 3.68-3.52 (m, 4H), 3.44-3.34 (m, 2H), 2.35 (dd, *J* = 8.1, 6.8 Hz, 2H), 1.66 (hex, *J* = 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.2, 158.5, 136.2, 128.7, 128.5, 128.3, 71.2, 70.7, 67.5,

65.8, 43.5, 36.2, 18.5, 13.8. HRMS (FAB+): *m/z* calculated for $[C_{16}H_{23}O_6N+H]^+$: 326.1604; found: 326.1613.

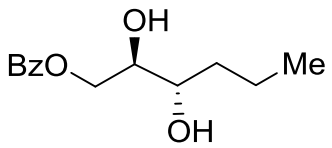


Anti-4-(((benzyloxy)carbonyl)amino)-2,3-dihydroxybutyl benzoate (6l): Synthesized according to general procedure E for cross metathesis – dihydroxylation using allyl benzoate as the olefin in excess. The title compound was purified by column chromatography (50-70% ethyl acetate in hexanes) to give a clear oil (19.9 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$-d_6) δ 8.06 (d, *J* = 6.8 Hz, 2H), 7.57 (ddt, *J* = 8.0, 7.0, 1.4 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.37-7.27 (m, 5H), 5.46 (d, *J* = 6.7 Hz, 1H), 5.1 (s, 2H), 4.64 (dd, *J* = 12.0, 4.8 Hz, 1H), 4.52 (dd, *J* = 12.0, 2.5 Hz, 1H), 3.82-3.73 (m, 2H), 3.67-3.53 (m, 3H), 3.41 (ddd, *J* = 15.3, 5.9, 2.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 158.6, 136.2, 133.6, 130.0, 129.6, 128.7, 128.6, 128.4, 128.3, 71.2, 70.9, 67.5, 66.5, 43.5. HRMS (FAB+): *m/z* calculated for $[C_{19}H_{21}O_6N+H]^+$: 360.1447; found: 360.1456.

Mechanistic experiments

*Dihydroxylation studies with (Z)-4-octene (**8**) and (Z)-but-2-ene-1,4-diyl diacetate (**7**):* A solution of $CeCl_3$ heptahydrate (3.7 mg, 0.01 mmol) in distilled H_2O (170 µL) was added to $NaIO_4$ (42.8 mg, 0.2 mmol). MeCN (500 µL) was then added, and the mixture was cooled to 0 °C in an ice bath. A solution of Ru catalyst **4** (0.001 mmol, 200 µL, 0.005 M in THF) was then added if required. Either (*Z*)-4-octene **8** (11.2 mg, 0.1 mmol) and/or (*Z*)-but-2-ene-1,4-diyl diacetate **7** (17.2 mg, 0.1 mmol) in ethyl acetate (0.5 ml) was then added. The mixture was vigorously stirred at 0 °C for 20 min and then quenched with 2 mL of a saturated $Na_2S_2O_3$ aqueous solution. The mixture was extracted with ethyl acetate (4 x 2.5 mL), and then concentrated under reduced pressure. Mesitylene was added as an internal standard (27.8 µL, 0.2 mmoL). The product distribution was analyzed by ^1H NMR.

Using (*Z*)-but-2-ene-1,4-diyl diacetate **7**, without Ru: No dihydroxylation observed.
Using (*Z*)-but-2-ene-1,4-diyl diacetate **7**, with Ru: *Anti*-diol **6b** was isolated in 58% yield (11.9 mg), and no olefin starting material remains.
Using (*Z*)-4-octene **8**, with Ru: No dihydroxylation products observed
Using (*Z*)-4-octene **8** and (*Z*)-but-2-ene-1,4-diyl diacetate **7**, with Ru: No dihydroxylation products observed.

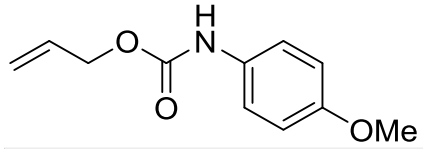


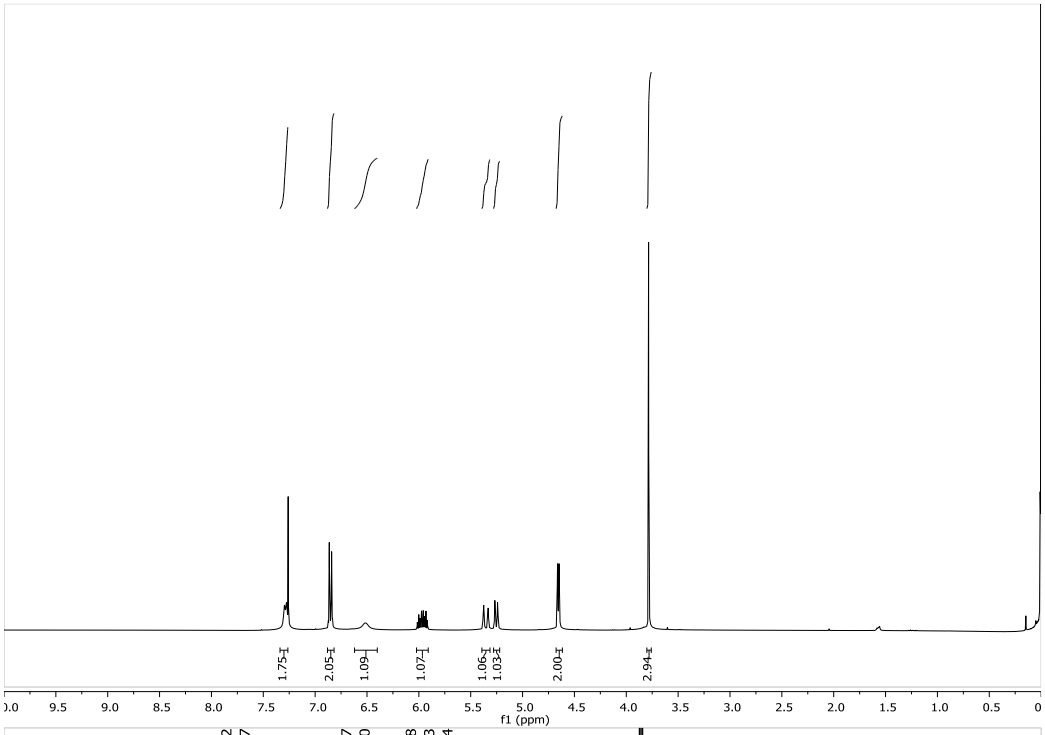
Anti-2,3-dihydroxyhexyl benzoate (10): In a nitrogen filled glove box, 1-pentene **9** (35.1 mg, 0.5 mmol, 5 eq) was added to allyl benzoate **5c** (16.2 mg,

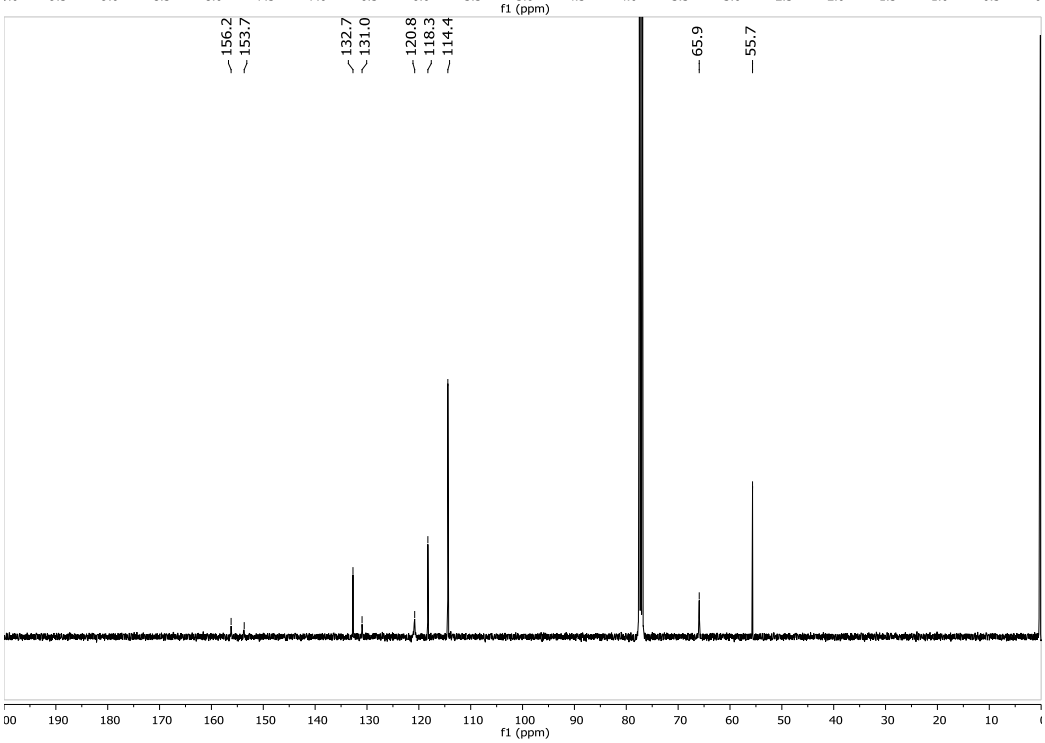
0.1 mmol, 1 eq) using Ad-DIPP-NO_3 **4** (0.003 mmol, 3 mol%, 150 µL, 0.02 M in THF) to quantitatively transfer to a Schlenk tube. The tube was capped, and then brought to a Schlenk line where it was evacuated using one freeze-pump-thaw cycle, capping the flask under static vacuum. The solution was then heated in an oil bath with stirring at 40 °C for 4 hr. Subsequently, the volatiles were removed with a high vacuum for 5 minutes. A solution of $CeCl_3$ heptahydrate (3.7 mg, 0.01 mmol, 10 mol%) in distilled H_2O (170 µL) was added to $NaIO_4$ (42.8 mg, 0.2 mmol, 2 eq relative to the homodimerization metathesis product at full conversion). MeCN (500 µL) was then added, and the mixture was cooled to 0 °C in an ice bath. The crude metathesis mixture was then added, using ethyl acetate (3 x 167 µL) to rinse the flask and ensure complete transfer. The mixture was vigorously stirred at 0 °C for 20 min and then quenched with 2 mL of a saturated $Na_2S_2O_3$ aqueous solution. The mixture was extracted with ethyl acetate (4 x 2.5 mL), and then concentrated under reduced pressure. The anti-diol product was purified using preparatory thin layer chromatography (one purification at 50% ethyl acetate in hexanes, then a second purification at 30% ethyl acetate in hexanes) to yield a clear oil (7.9 mg, 33%). If this procedure is followed without removing volatiles after the metathesis step, no dihydroxylation is observed – only cross metathesis products. ^{1}H NMR (500 MHz, $CDCl_3$-d_6) δ 8.05 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.59 (ddt, *J* = 7.7, 7.3, 1.4 Hz, 1H), 7.46 (tt, *J* = 8.0, 1.5 Hz, 1H), 4.52 (s, 1H), 4.51 (d, *J* = 1.2 Hz, 1H), 3.91 (q, *J* = 4.9 Hz, 1H), 3.80-3.74 (m, 1H), 2.64 (br s, 1H), 2.22 (br s, 1H), 1.65-1.50 (m, 3H), 1.45-1.37 (m, 1H), 0.97 (t, *J* = 7.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 133.5, 129.9, 129.8, 128.6,

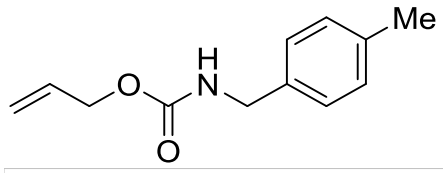
73.3, 72.4, 66.3, 34.7, 19.2, 14.2; HRMS (FAB+): *m/z* calculated for $[C_{13}H_{18}O_4+H]^+$: 239.1283; found: 239.1285.

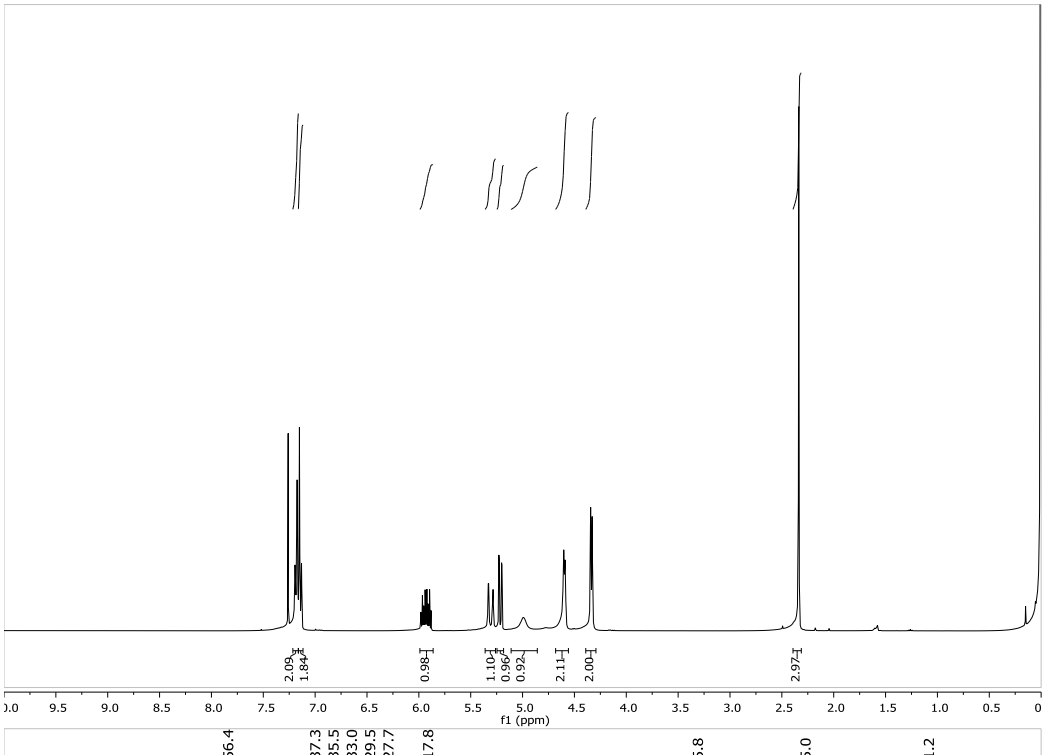
Spectra

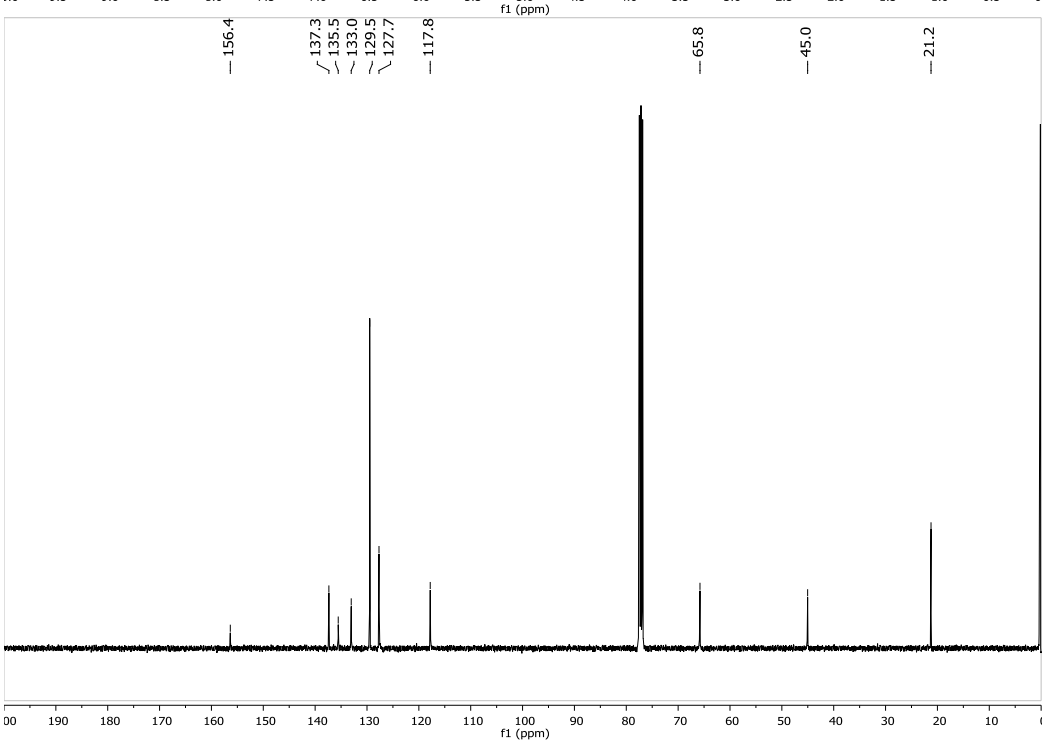

H
N
O
O
OMe

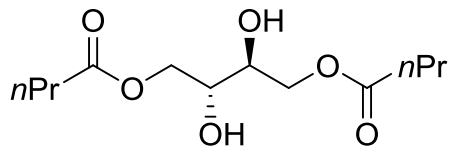

1.75
2.05
1.09
1.07
1.06
1.03
2.00
2.94
f1 (ppm)

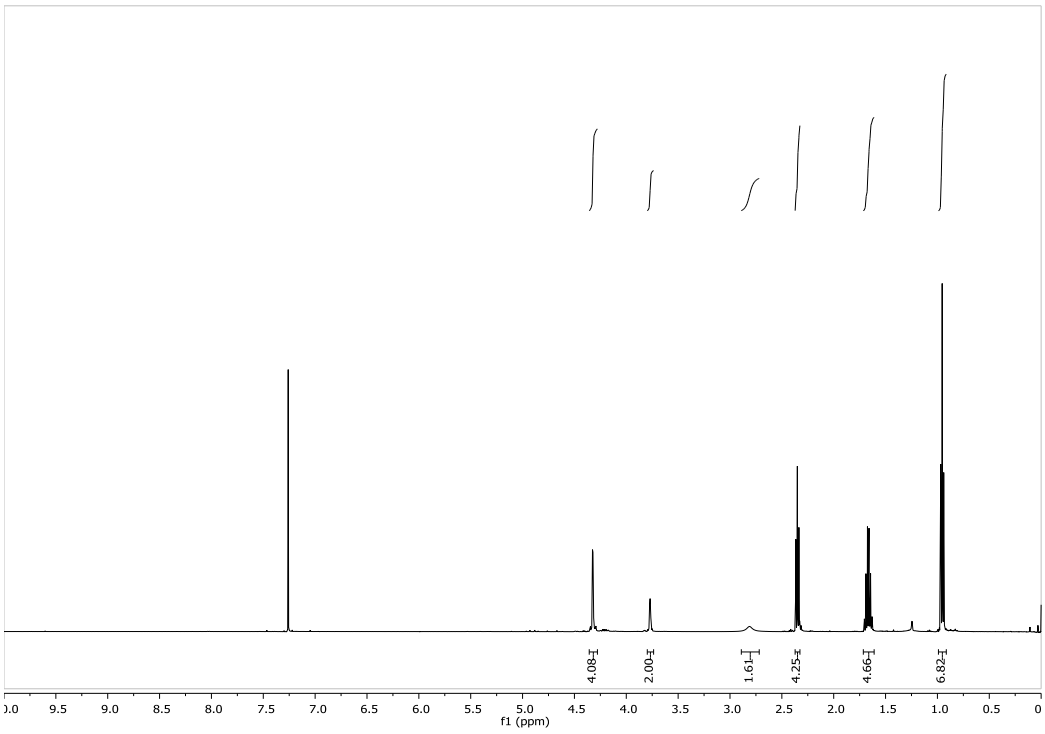

156.2
153.7
132.7
131.0
120.8
118.3
114.4
65.9
55.7
f1 (ppm)

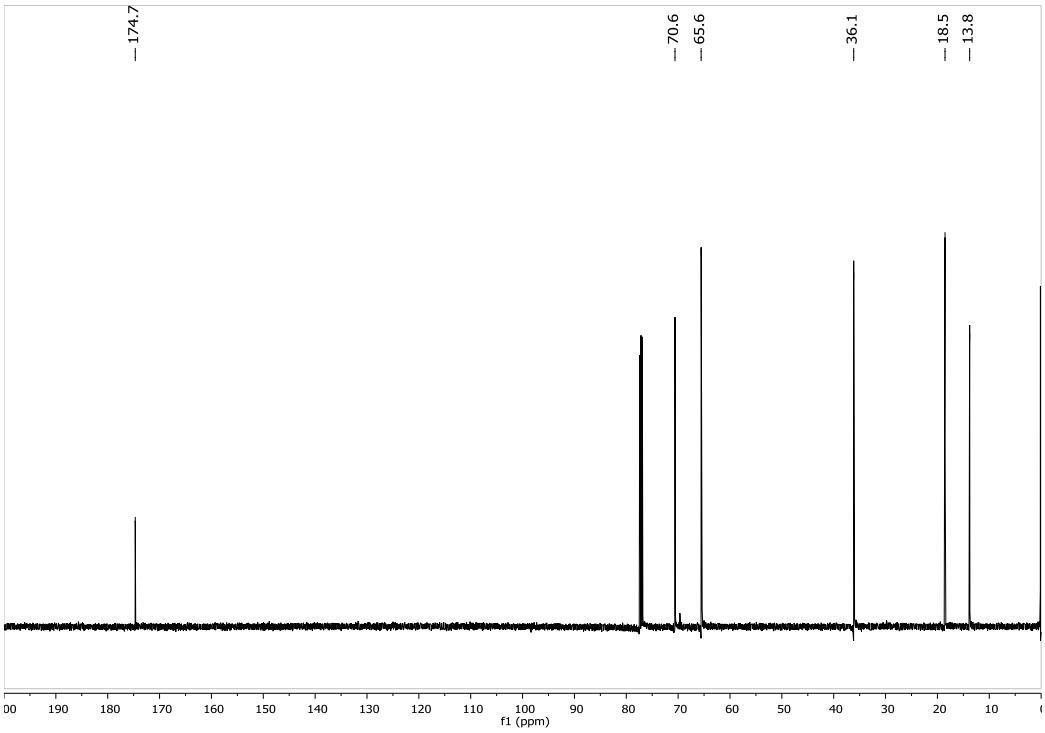

Me
H
N
O
O

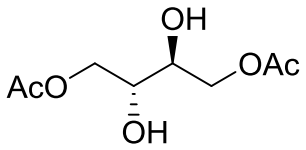

2.09
1.84
0.98
1.10
0.96
0.92
2.11
2.00
2.97
f1 (ppm)

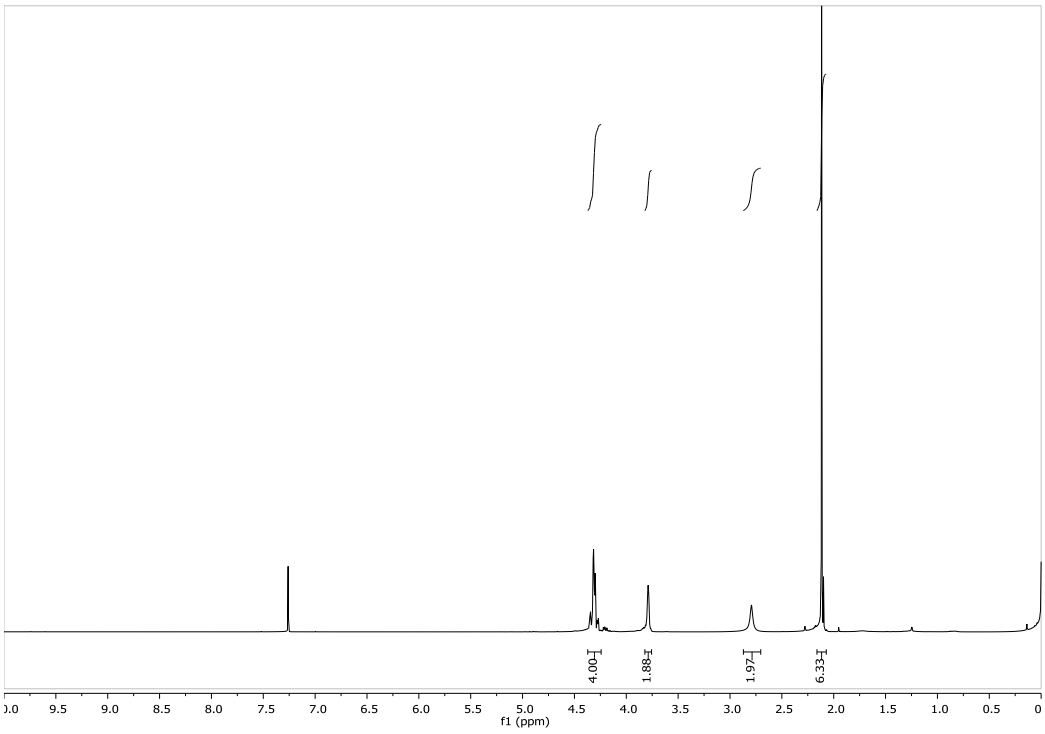

156.4
137.3
135.5
133.0
129.5
127.7
117.8
65.8
45.0
21.2
f1 (ppm)

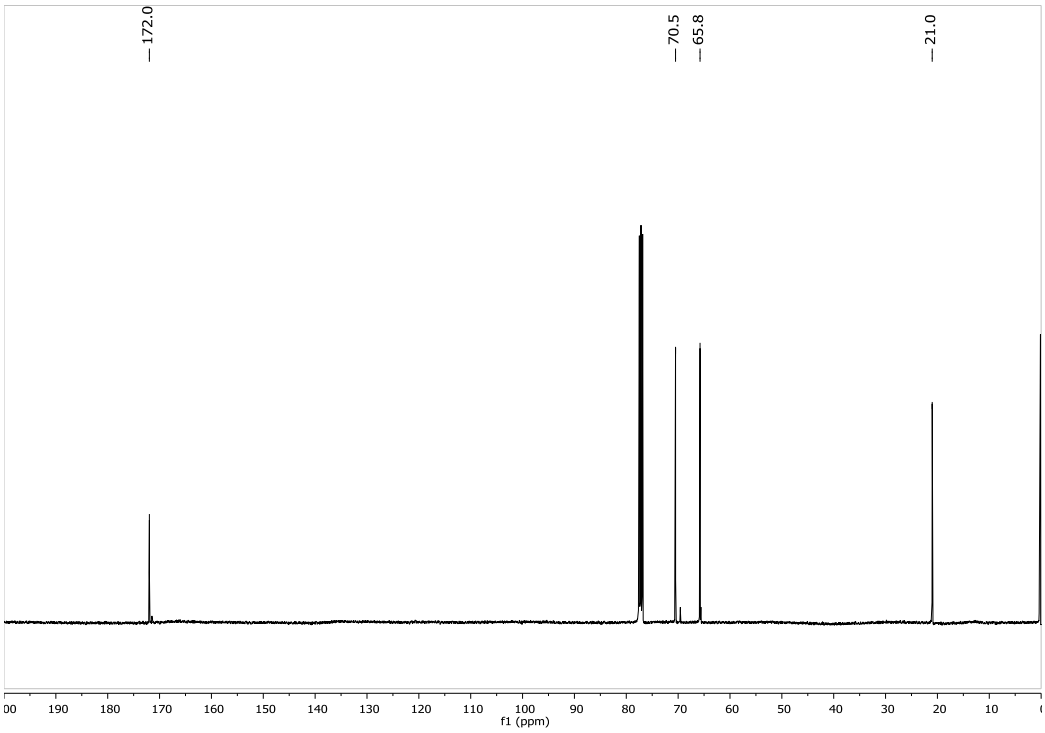

O
OH
nPr
O
O
nPr
OH
O

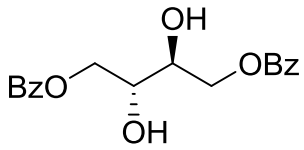

4.08
2.00
1.61
4.25
4.66
6.82
f1 (ppm)

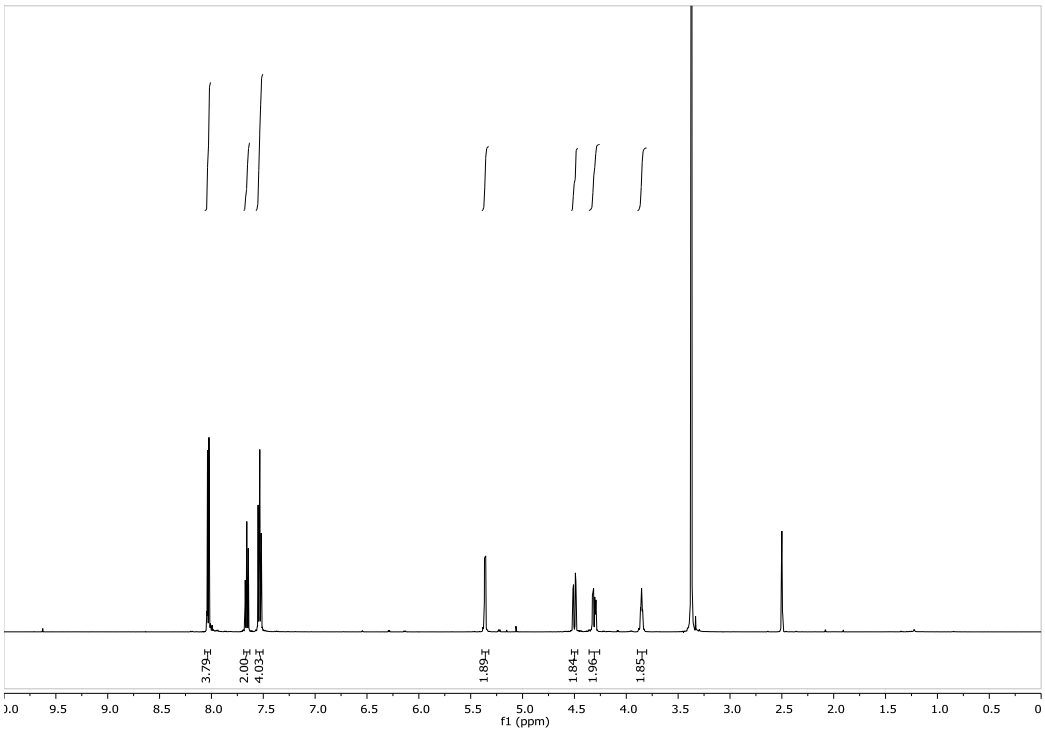

174.7
70.6
65.6
36.1
18.5
13.8
f1 (ppm)

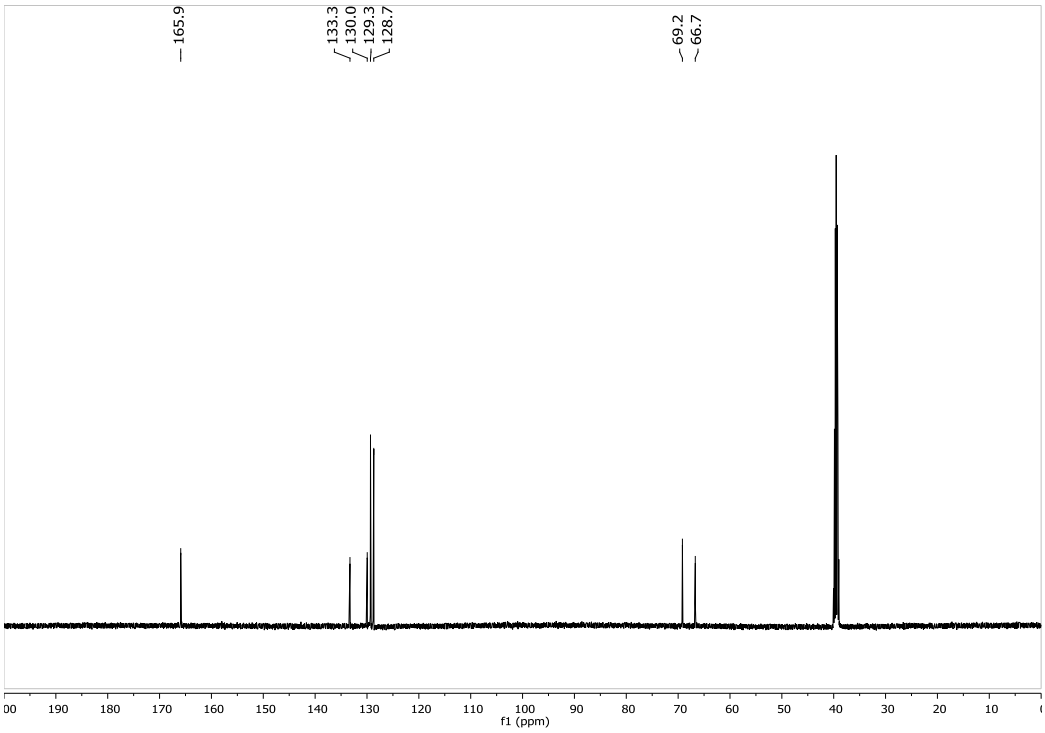

OH
AcO
OAc
OH

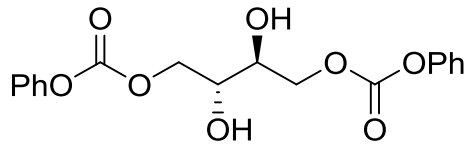

4.00
1.88
1.97
6.33
f1 (ppm)


172.0
70.5
65.8
21.0
f1 (ppm)

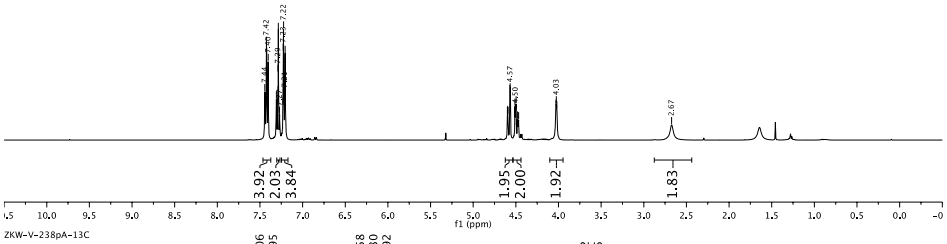

OH
OBz
BzO
OH


3.79
2.00
4.03
1.89
1.84
1.96
1.85
f1 (ppm)

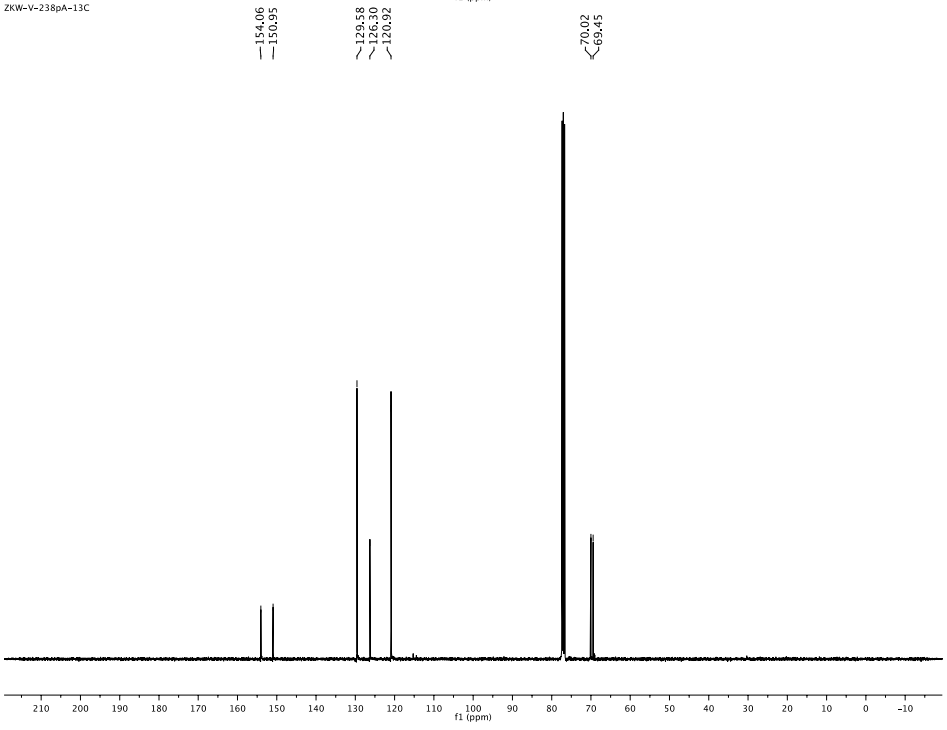

165.9
133.3
130.0
129.3
128.7
69.2
66.7
f1 (ppm)

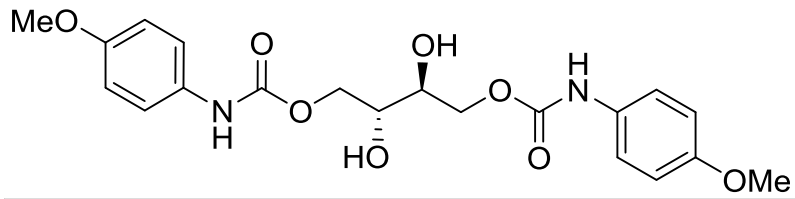


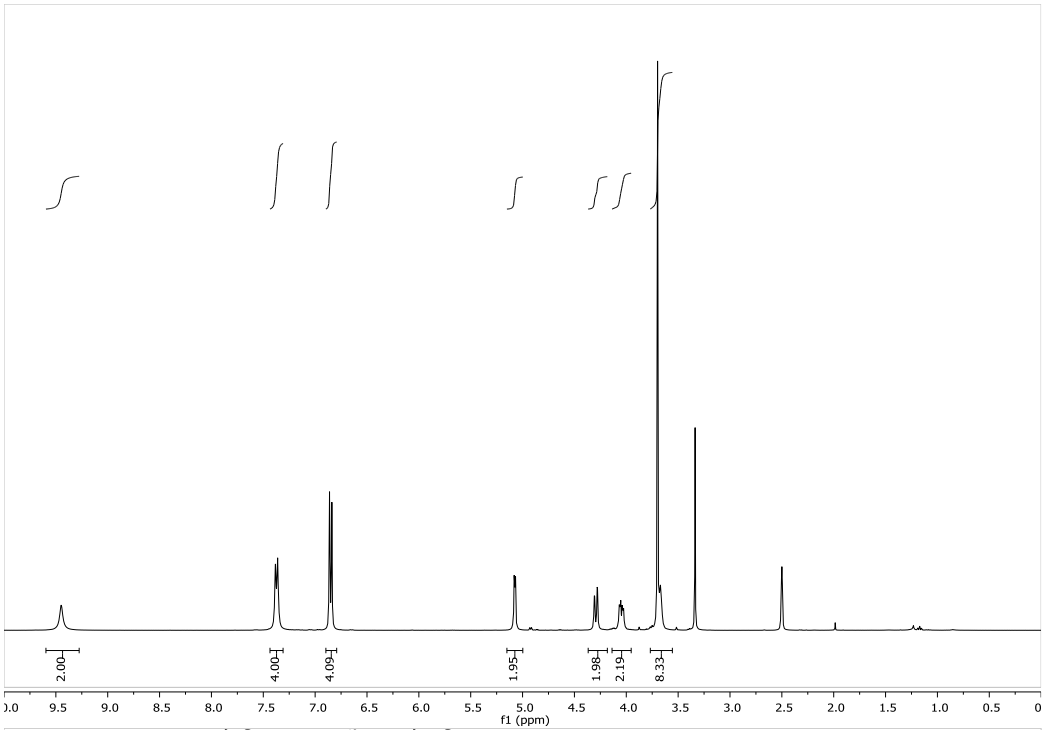
ZKW-V-238pA1

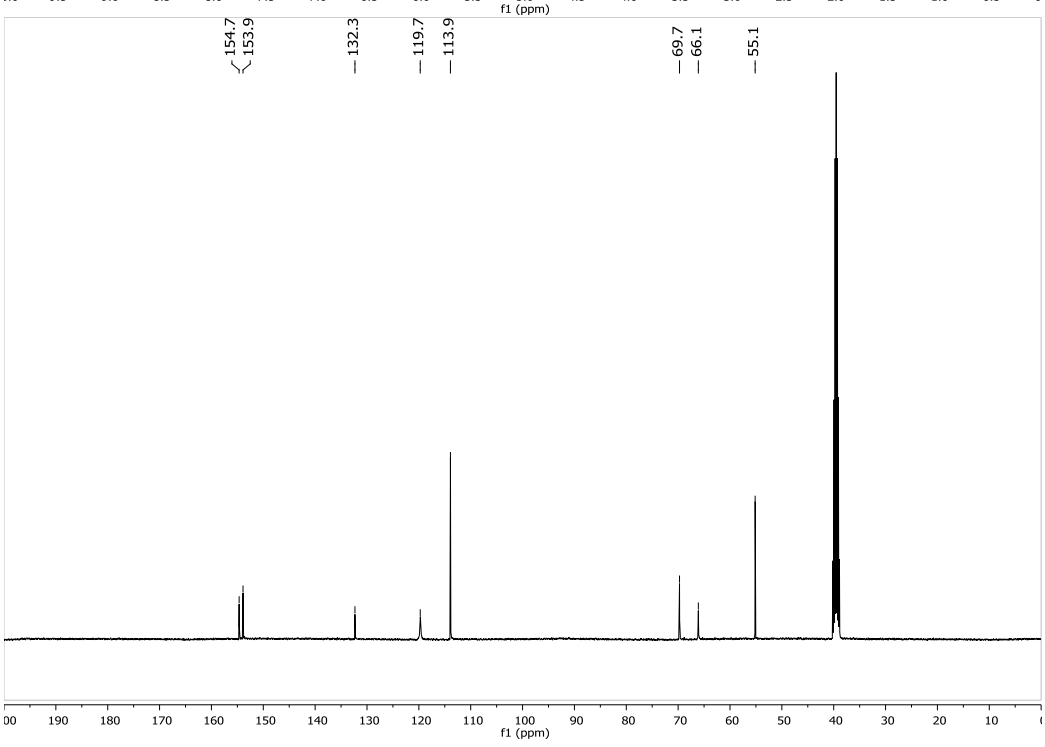


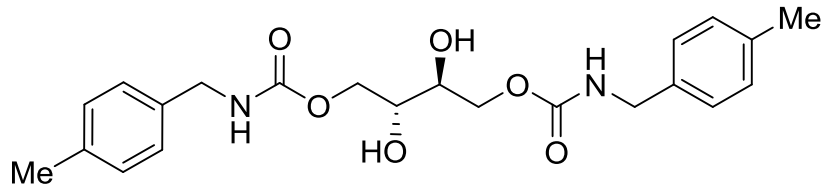
ZKW-V-238pA-13C

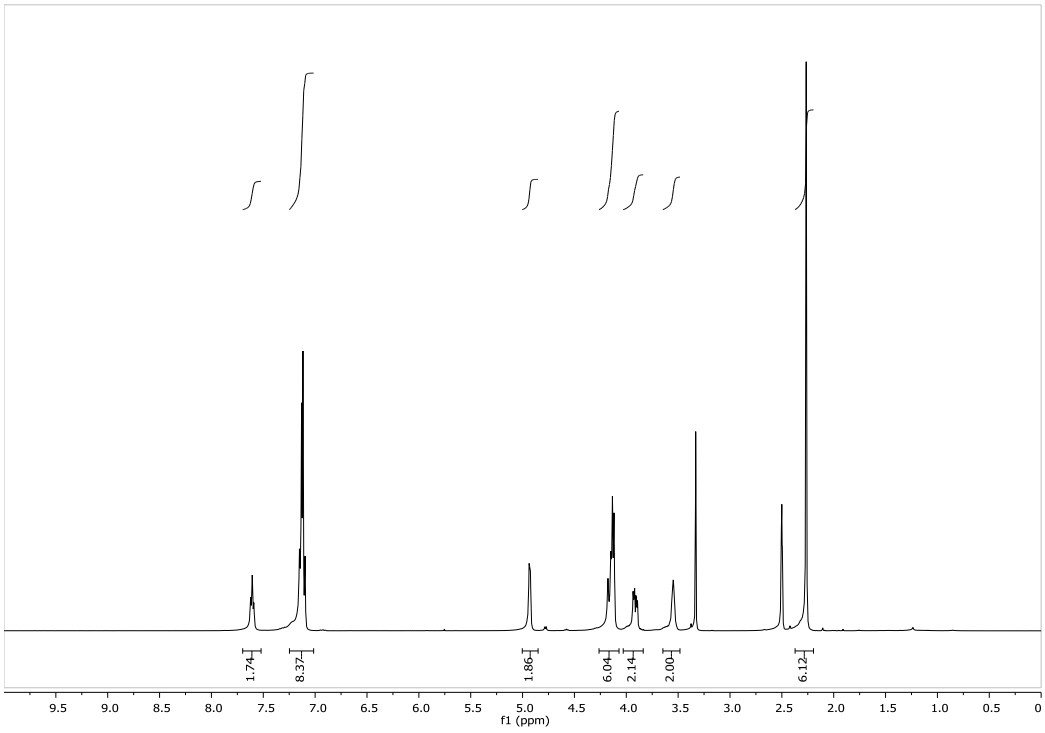


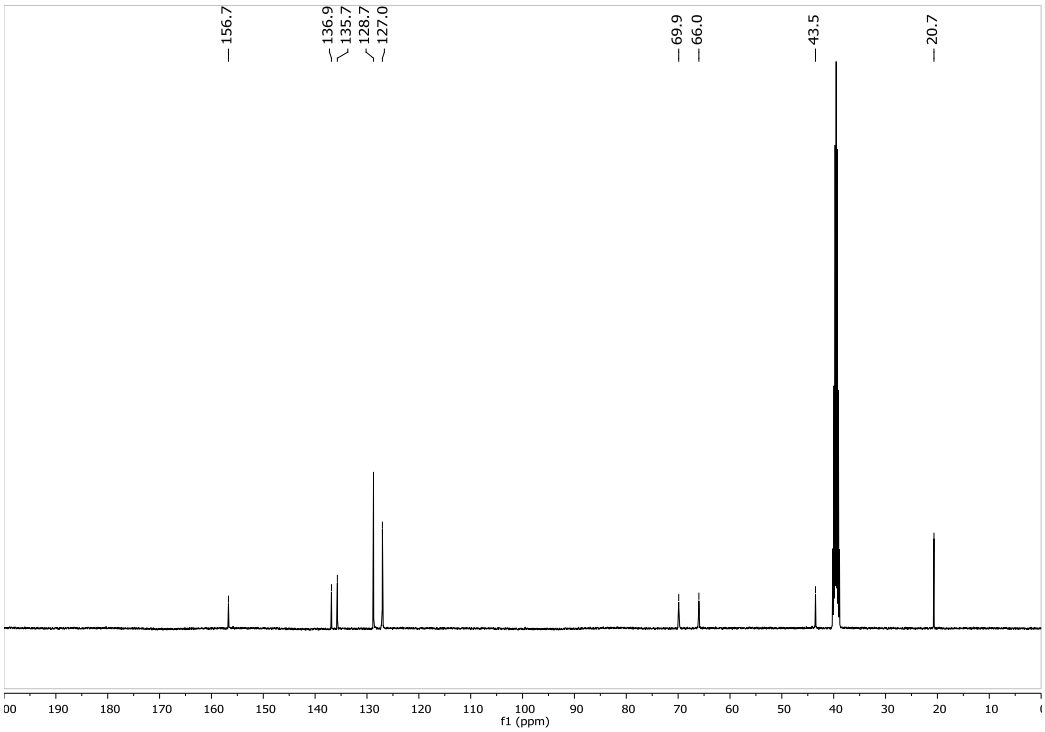

MeO
O
N
H
O
OH
HO
O
H
N
O
OMe

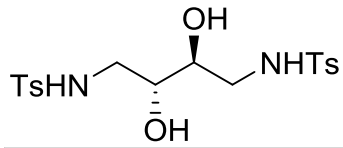

2.00
4.00
4.09
1.95
1.98
2.19
8.33
f1 (ppm)

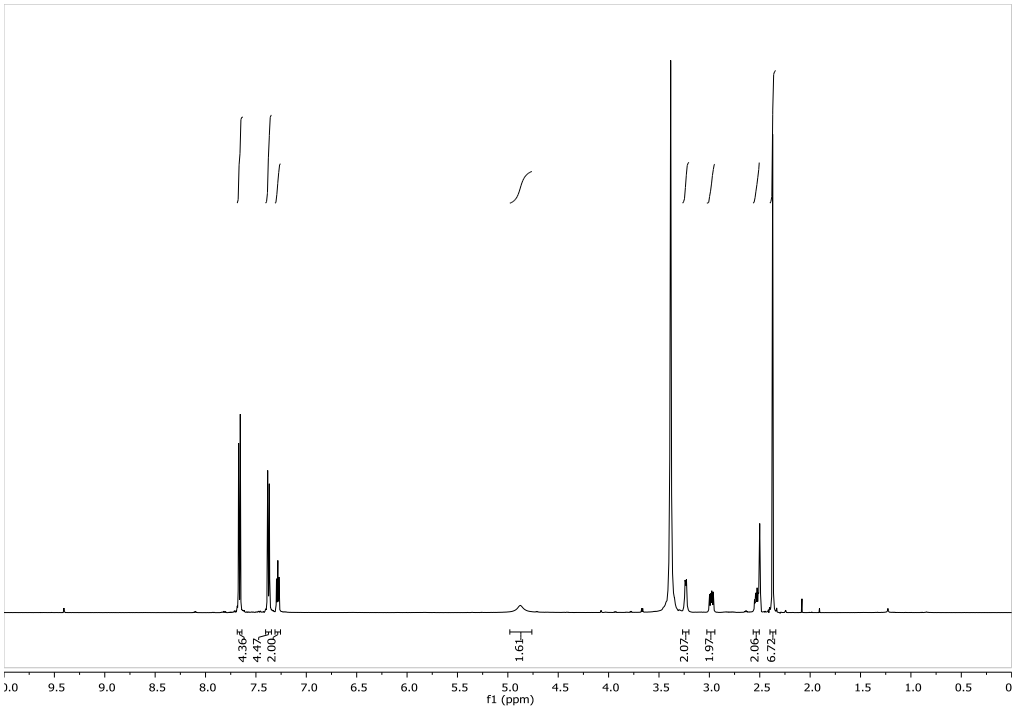

154.7
153.9
132.3
119.7
113.9
69.7
66.1
55.1
f1 (ppm)

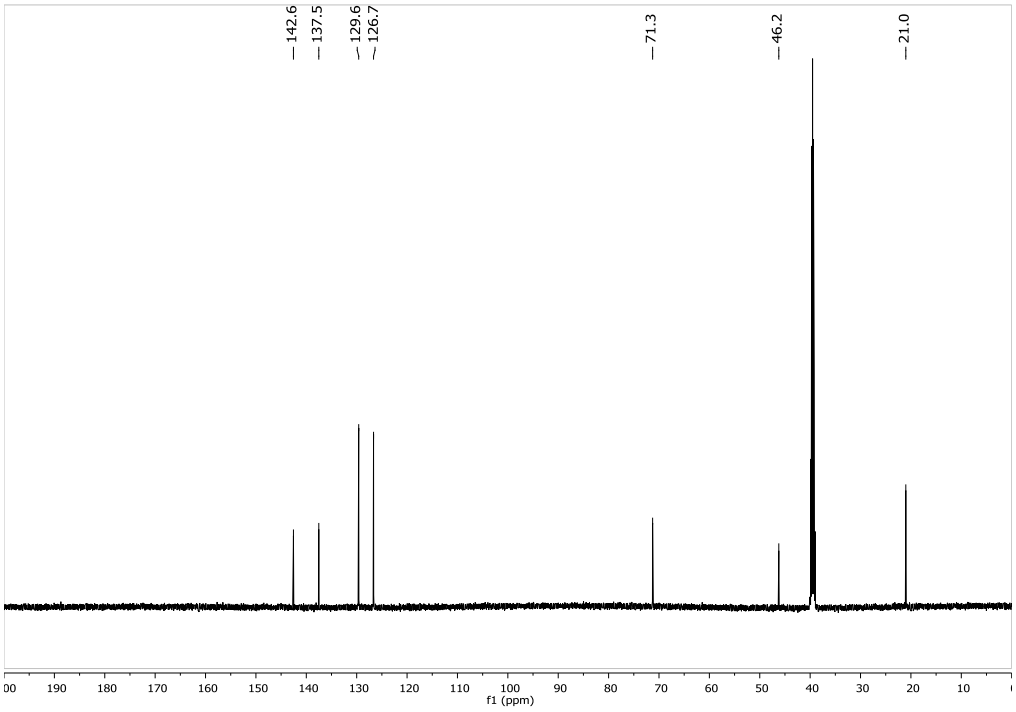

Me
O
OH
H
N
O
N
H
O
HO
O
Me

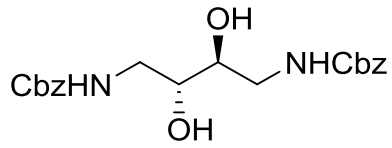

1.74
8.37
1.86
6.04
2.14
2.00
6.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

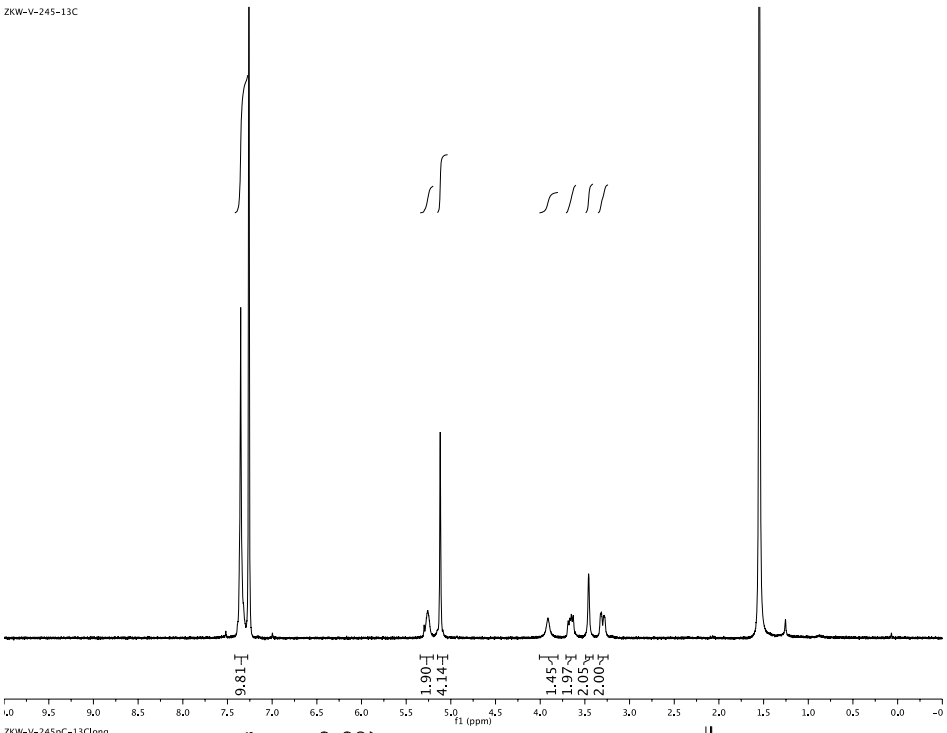

156.7
136.9
135.7
128.7
127.0
69.9
66.0
43.5
20.7
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

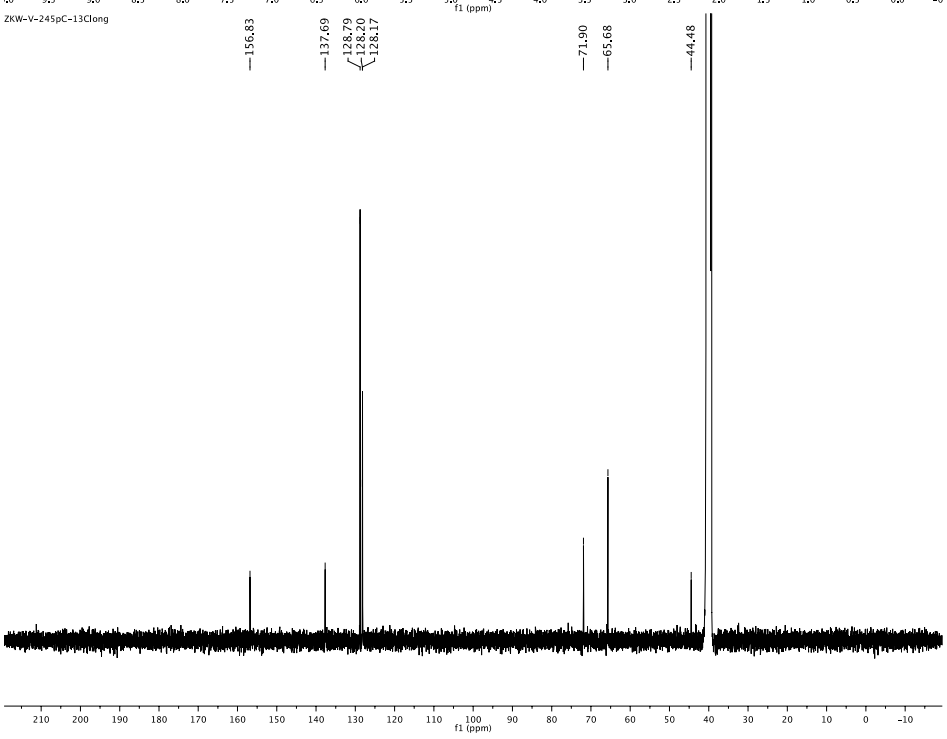

OH
NHTs
TsHN
OH

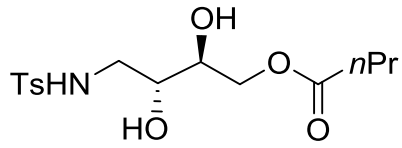

4.36
4.47
2.00
1.61
2.07
1.97
2.06
6.72
f1 (ppm)

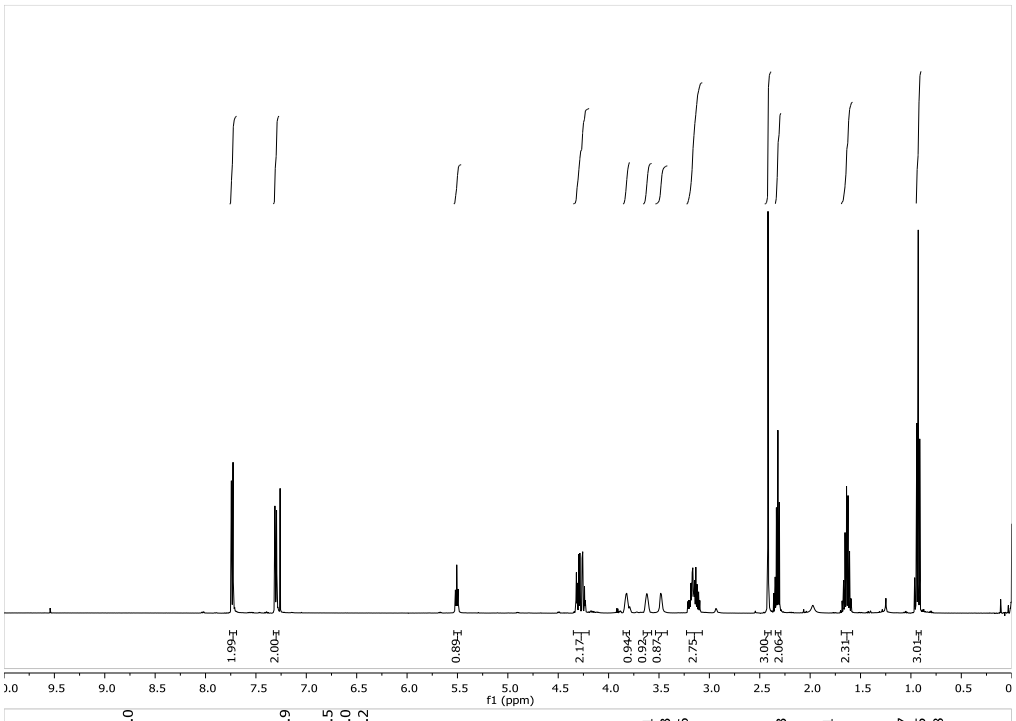

142.6
137.5
129.6
126.7
71.3
46.2
21.0
f1 (ppm)

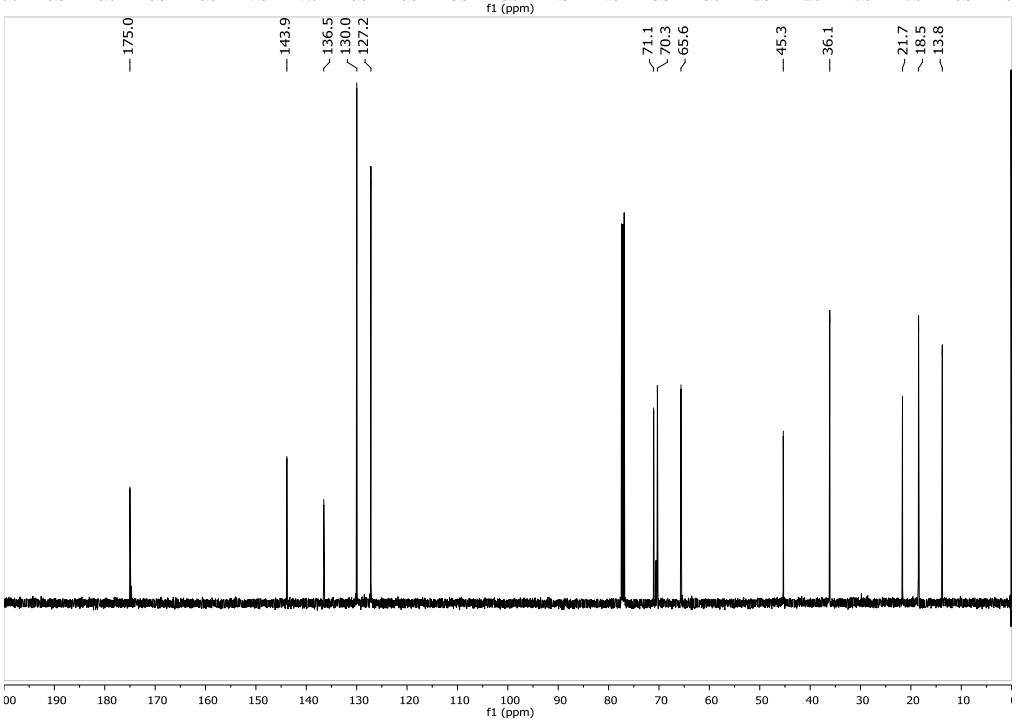

OH
CbzHN
NHCbz
OH

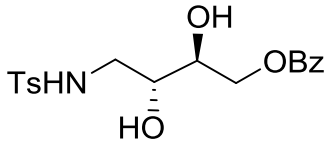

ZKW-V-245-13C
9.81
1.90
4.14
1.45
1.97
2.05
2.00
f1 (ppm)

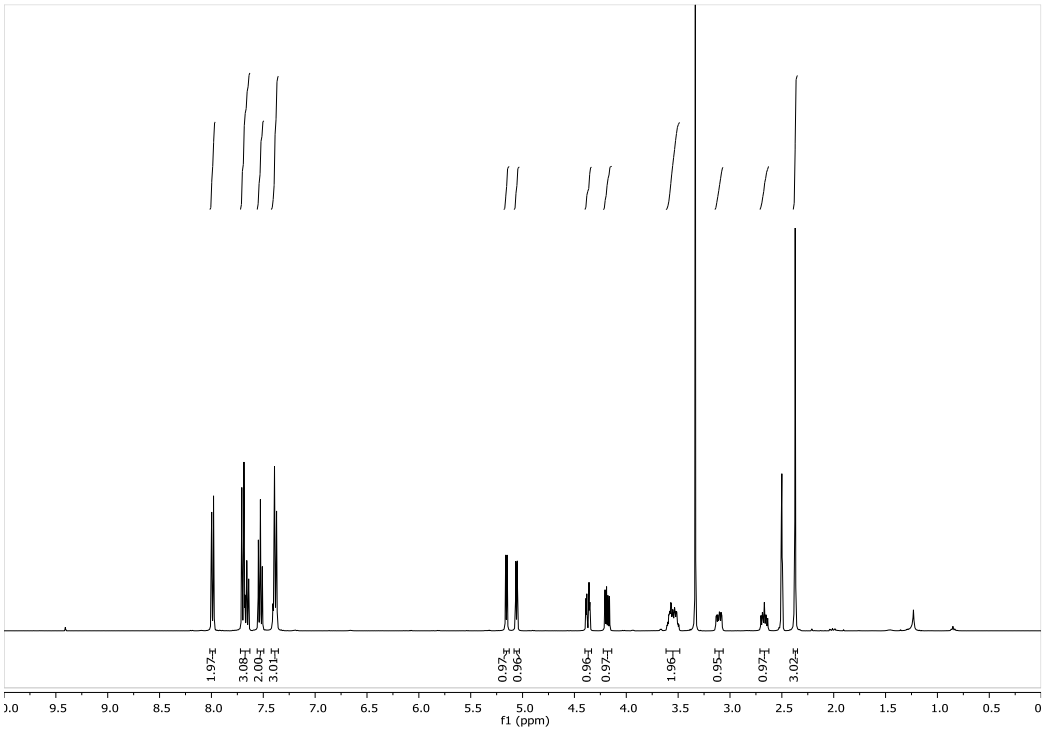

ZKW-V-245pC-13Clong
156.83
137.69
128.79
128.20
128.17
71.90
65.68
44.48
f1 (ppm)

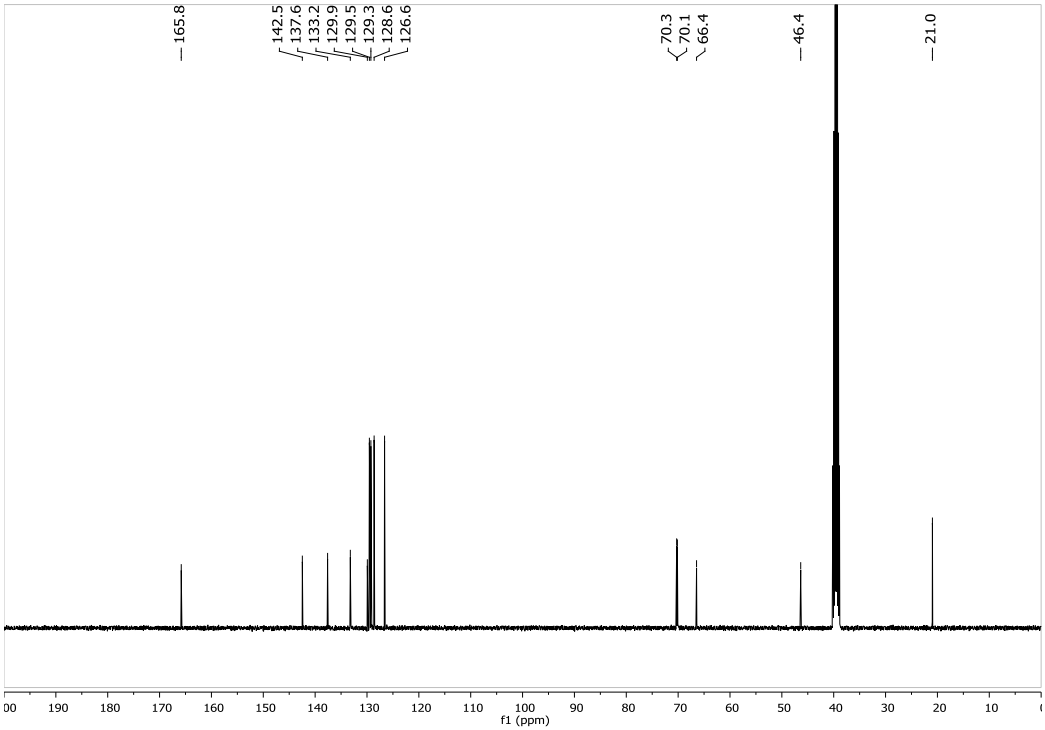

OH
TsHN
O
nPr
HO
O

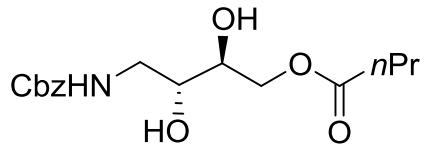

1.99
2.00
0.89
2.17
0.94
0.92
0.87
2.75
3.00
2.06
2.31
3.01
f1 (ppm)

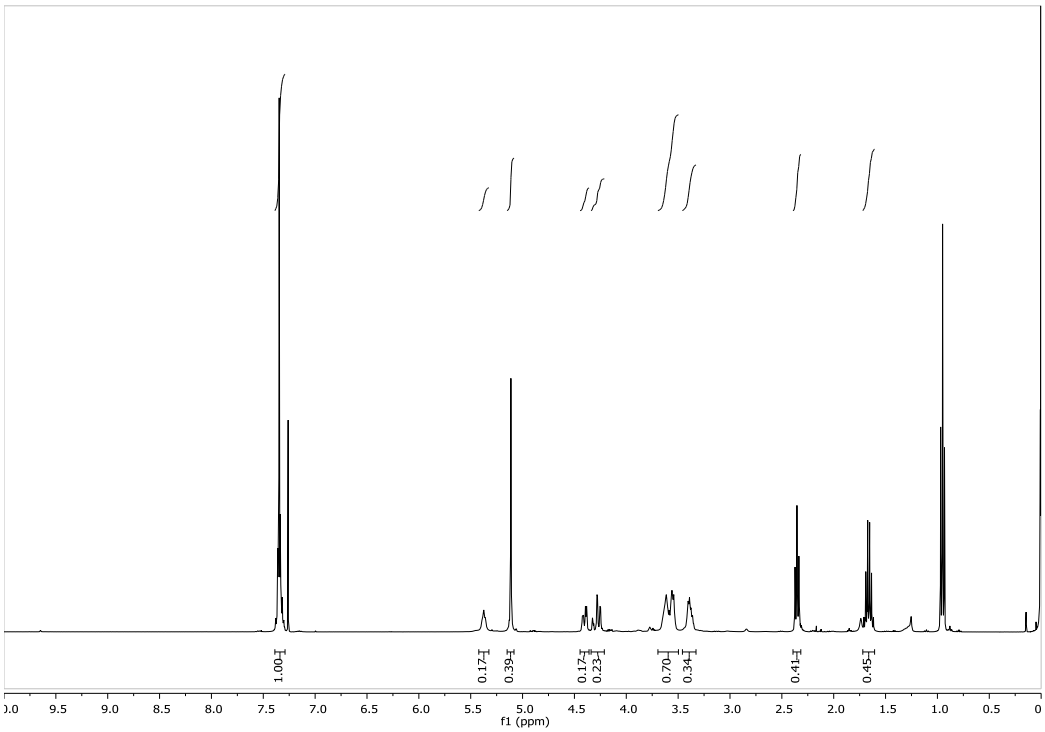

175.0
143.9
136.5
130.0
127.2
71.1
70.3
65.6
45.3
36.1
21.7
18.5
13.8
f1 (ppm)

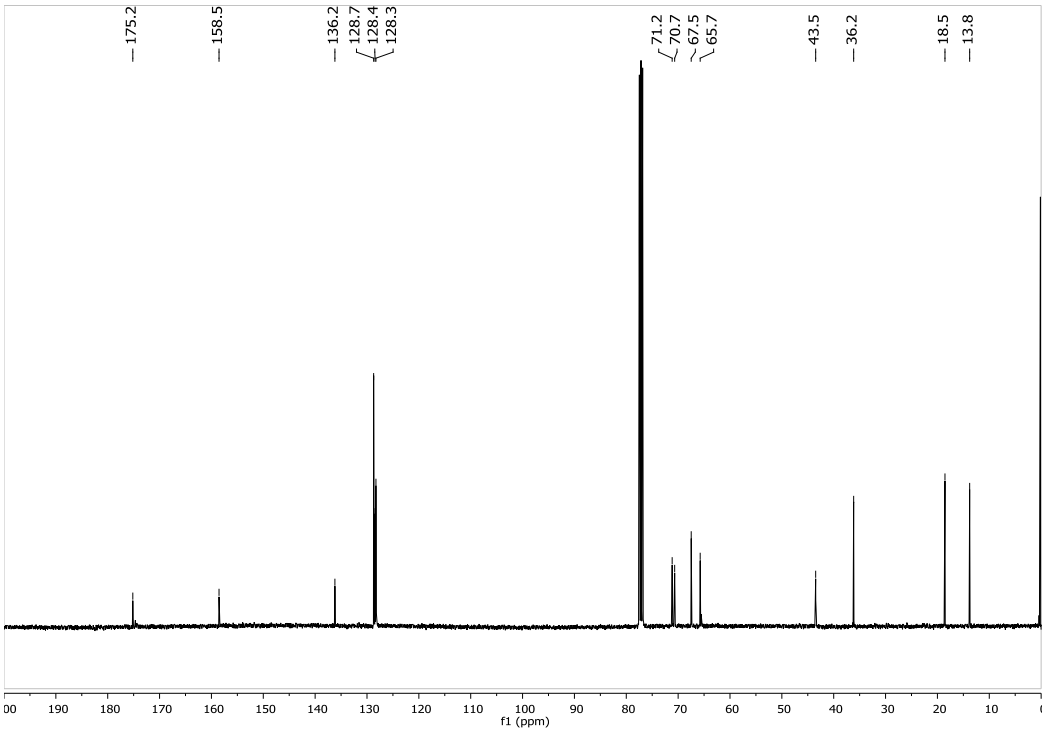

OH
OBz
TsHN
HO

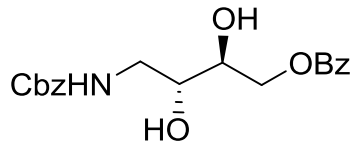

1.97
3.08
2.00
3.01
0.97
0.96
0.96
0.97
1.96
0.95
0.97
3.02
f1 (ppm)

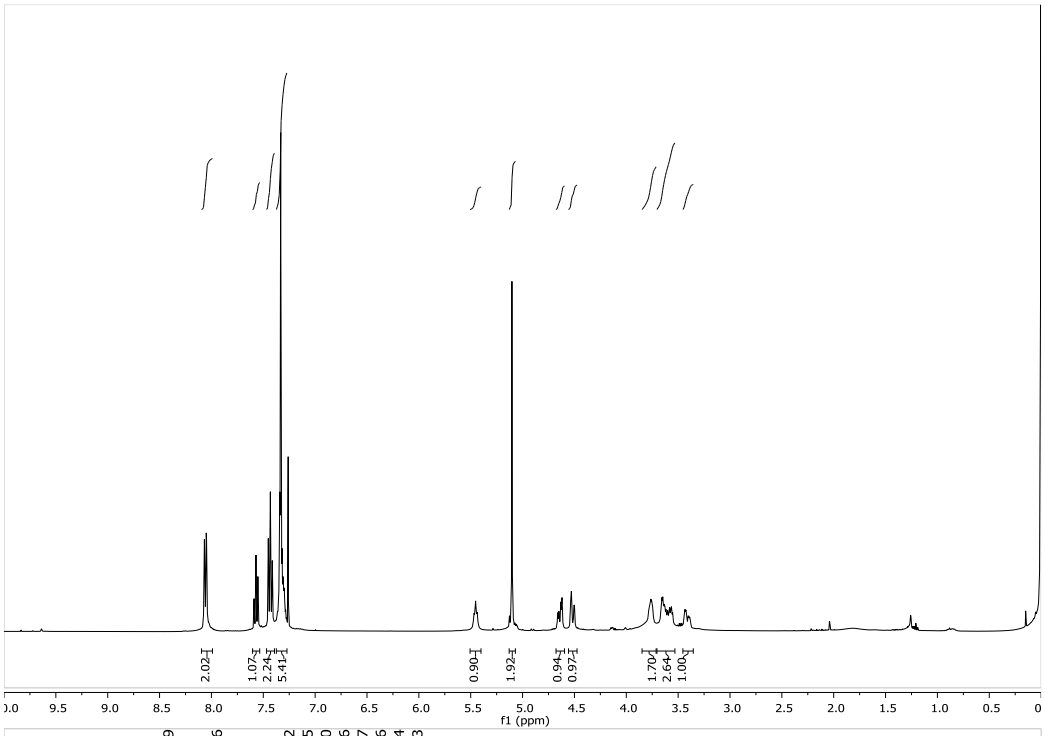

165.8
142.5
137.6
133.2
129.9
129.5
129.3
128.6
126.6
70.3
70.1
66.4
46.4
21.0
f1 (ppm)

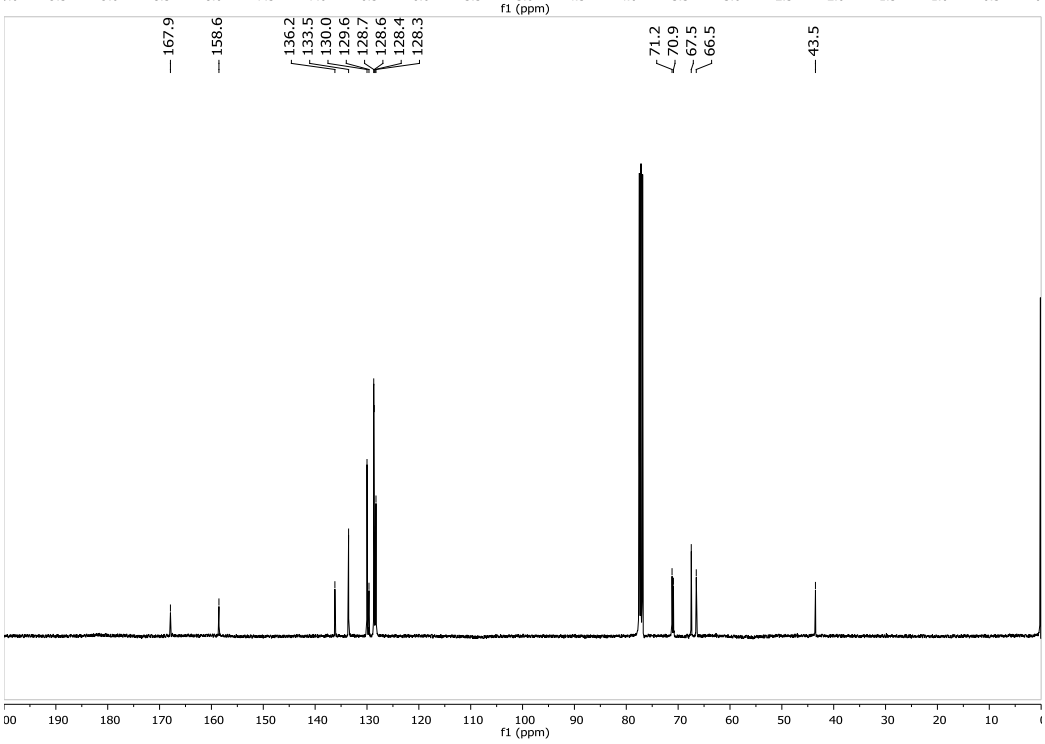

OH
CbzHN
O
nPr
HO
O

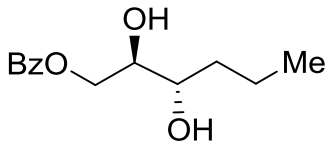

1.00
0.17
0.39
0.17
0.23
0.70
0.34
0.41
0.45
f1 (ppm)

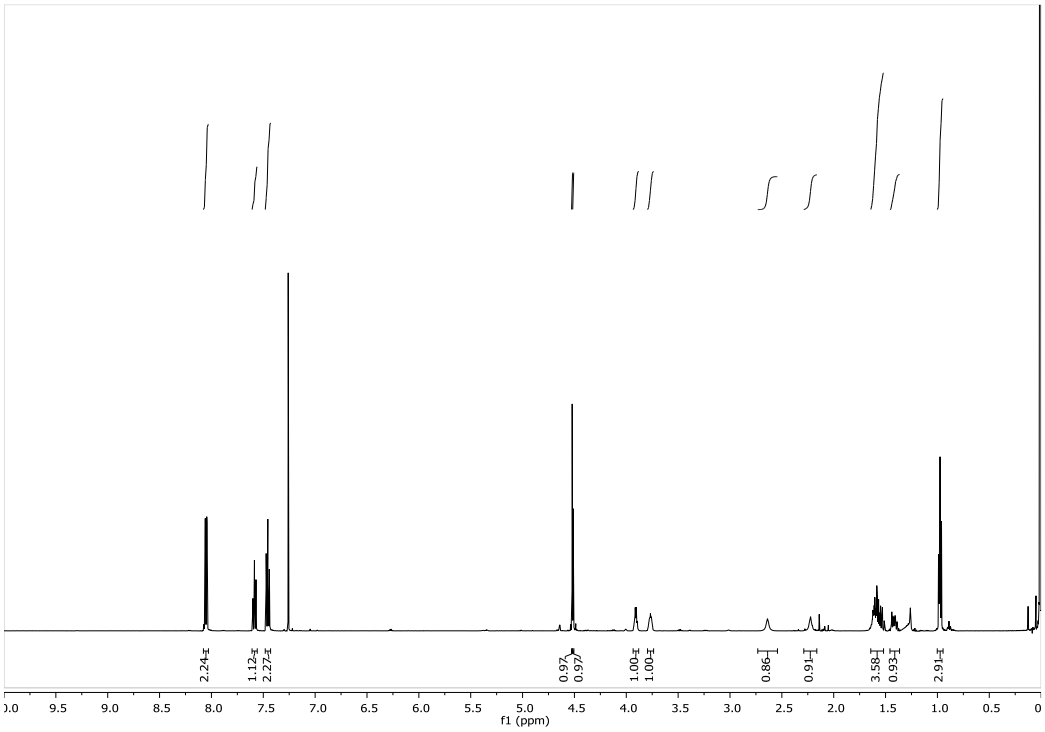

175.2
158.5
136.2
128.7
128.4
128.3
71.2
70.7
67.5
65.7
43.5
36.2
18.5
13.8
f1 (ppm)

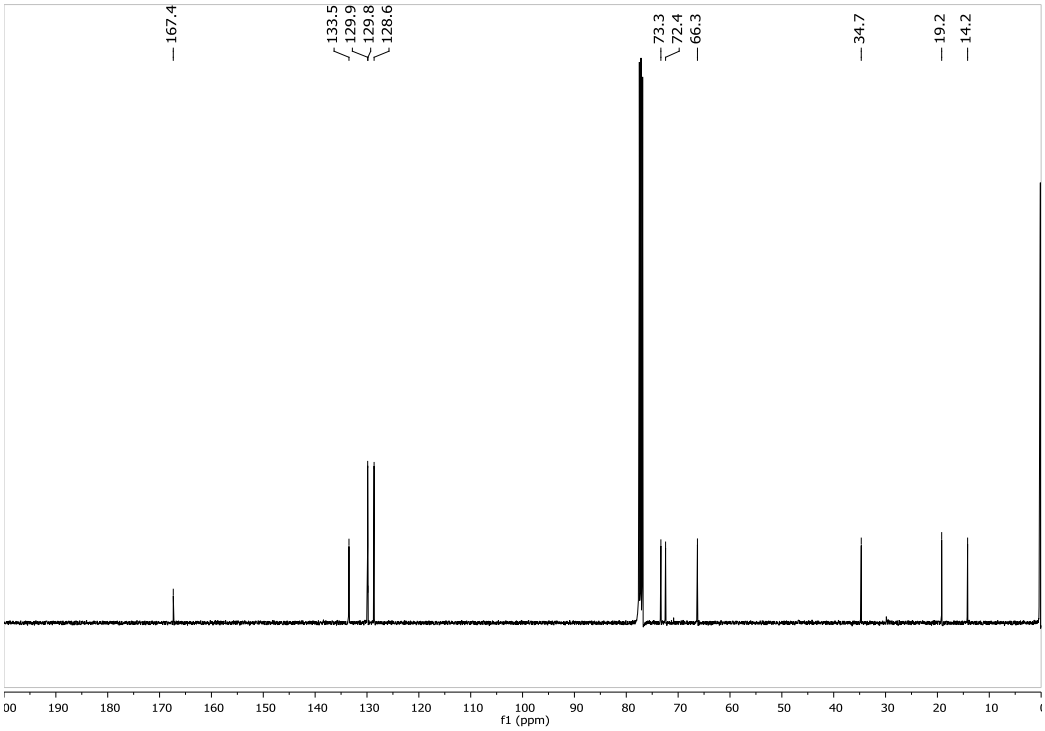

OH
CbzHN
OBz
HO


2.02
1.07
2.24
5.41
0.90
1.92
0.94
0.97
1.70
2.64
1.00
f1 (ppm)


167.9
158.6
136.2
133.5
130.0
129.6
128.7
128.6
128.4
128.3
71.2
70.9
67.5
66.5
43.5
f1 (ppm)


OH
BzO
Me
OH


2.24
1.12
2.27
0.97
0.97
1.00
1.00
0.86
0.91
3.58
0.93
2.91
f1 (ppm)


167.4
133.5
129.9
129.8
128.6
73.3
72.4
66.3
34.7
19.2
14.2
f1 (ppm)